# Armed Forces College of Medicine

## AFCM

# Immunoglobulin isotypes

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# Humoral Immune response

## By the end of this lecture the student will be able to*:*

1. Differentiate between the sequence of B cell activation in T cell dependent
   & T cell independent antigens

2. Compare between primary and secondary humoral immune response.

3.Discriminate between different isotypes of immunoglobulins regarding structure, distribution and function

4.Outline monoclonal Abs

# Immunoglobulins

## Structure

- Arranged in 3 fragments: قطع

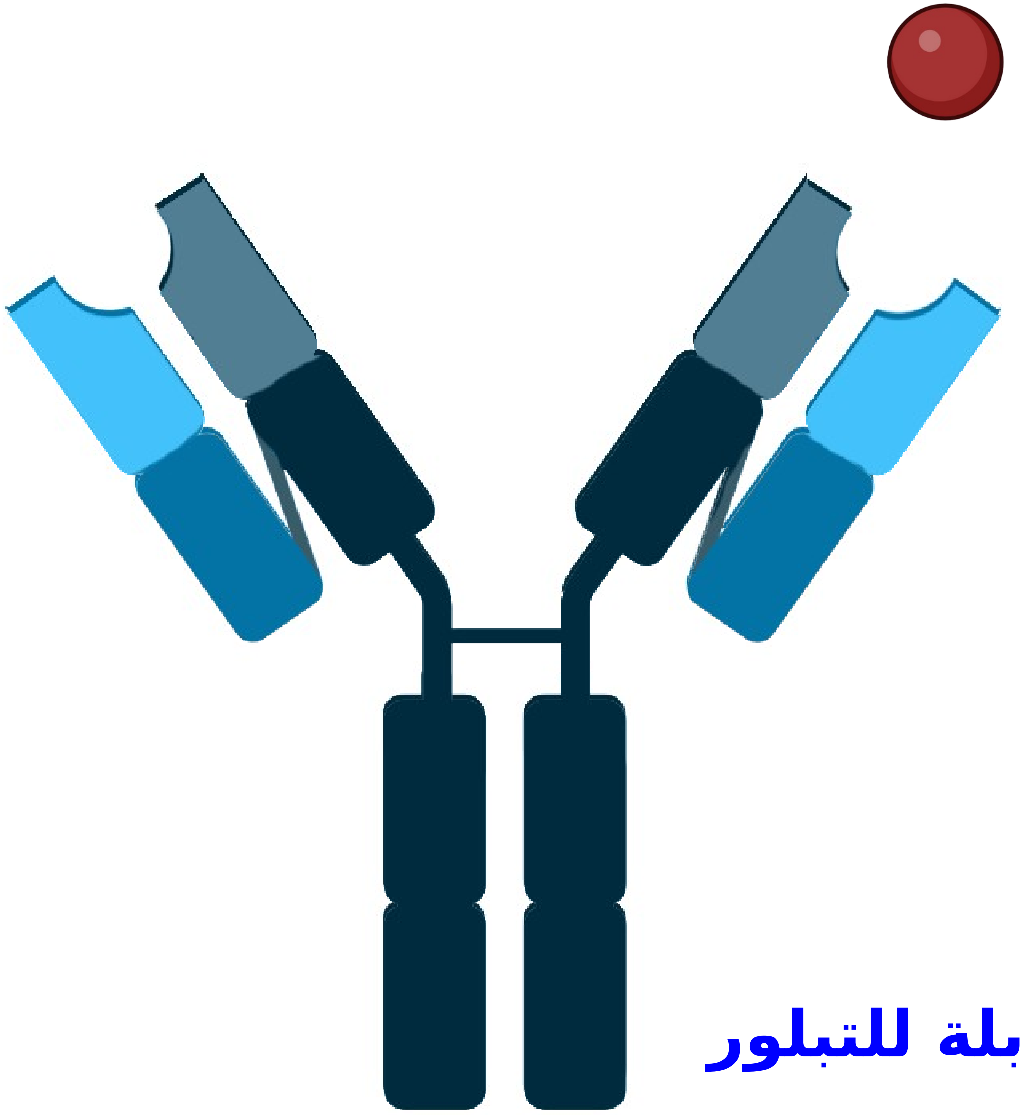
  2 Identical Ag binding sites (2 Fab)

  & 1 crystallizable (Fc)

- Each chain is formed of :

  Variable (V) region

  & Constant (C) region

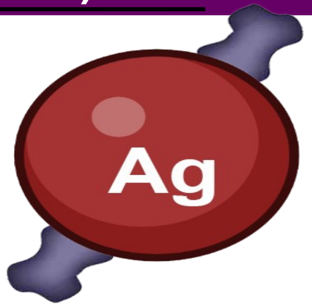


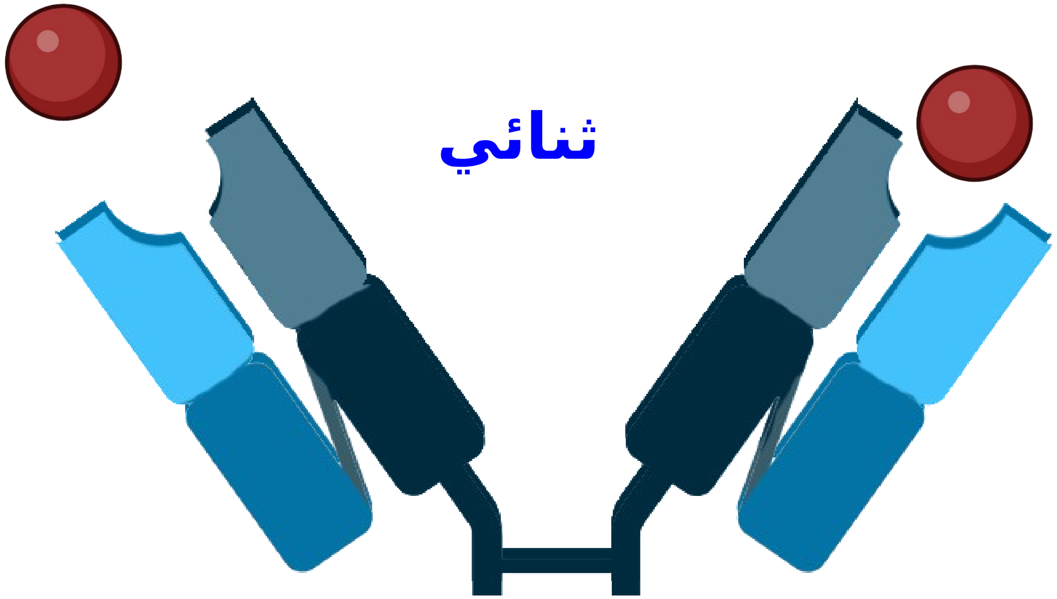
قابلة للتبلور

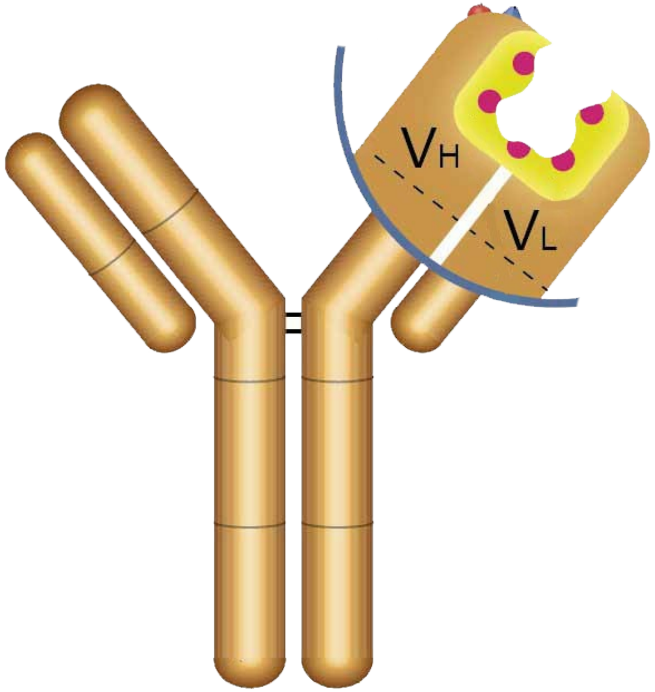
وحدة قاعدية     Monomer or basic unit

# Heavy & light chains

## Variable region (in Fab)

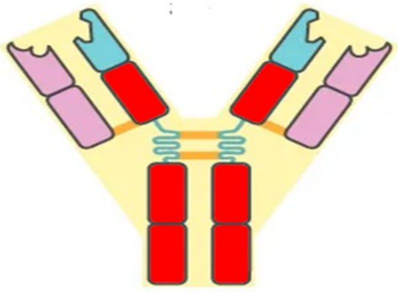


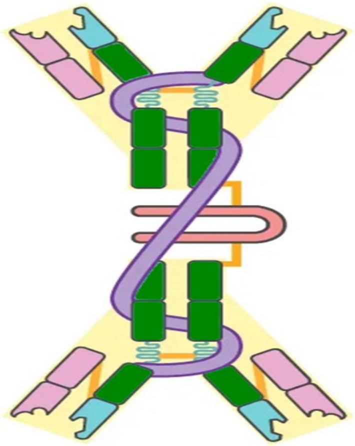


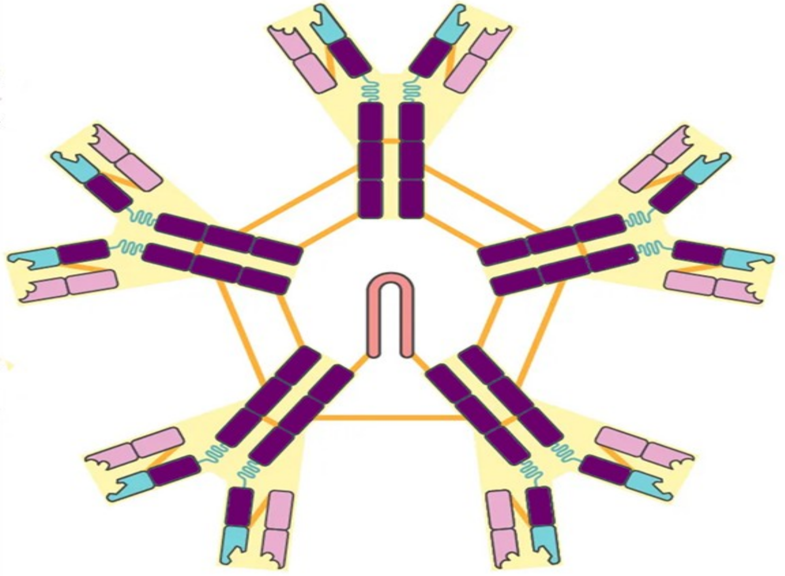


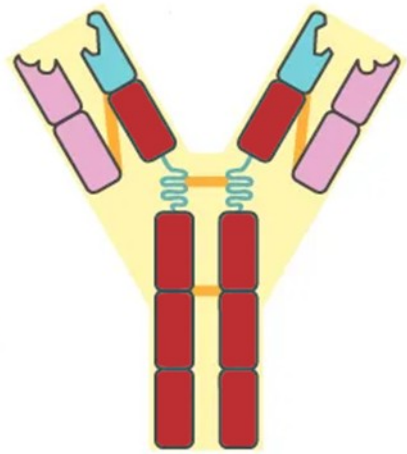
# Constant region of Heavy chain

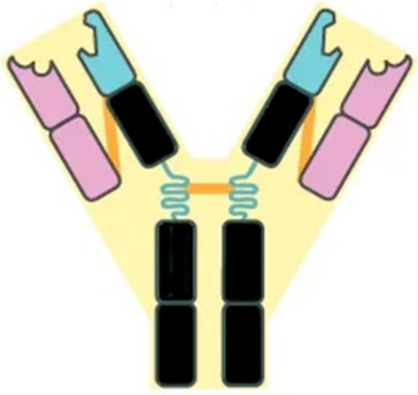
**Name of constant heavy chain**



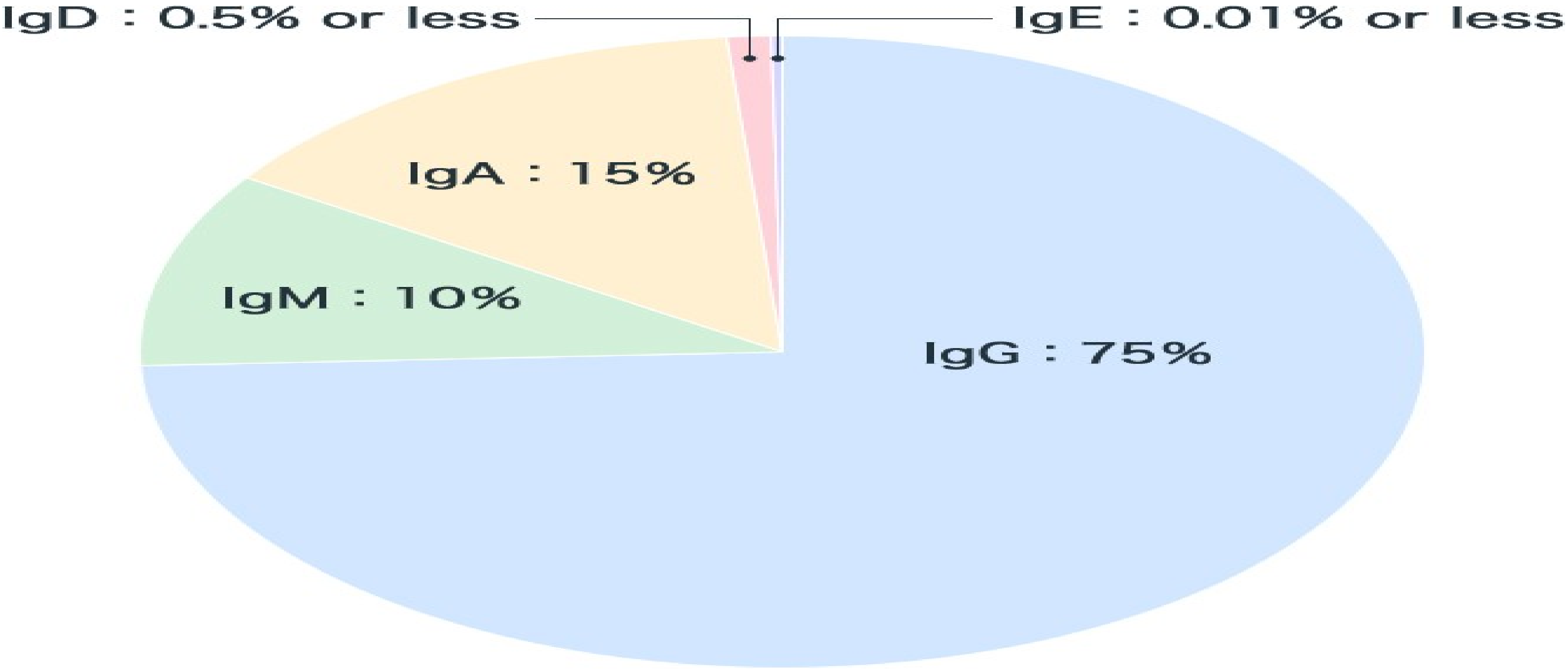




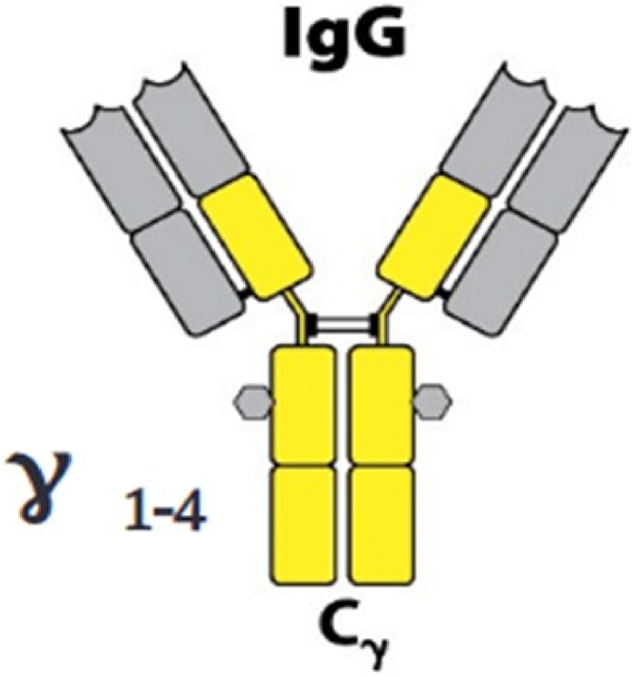


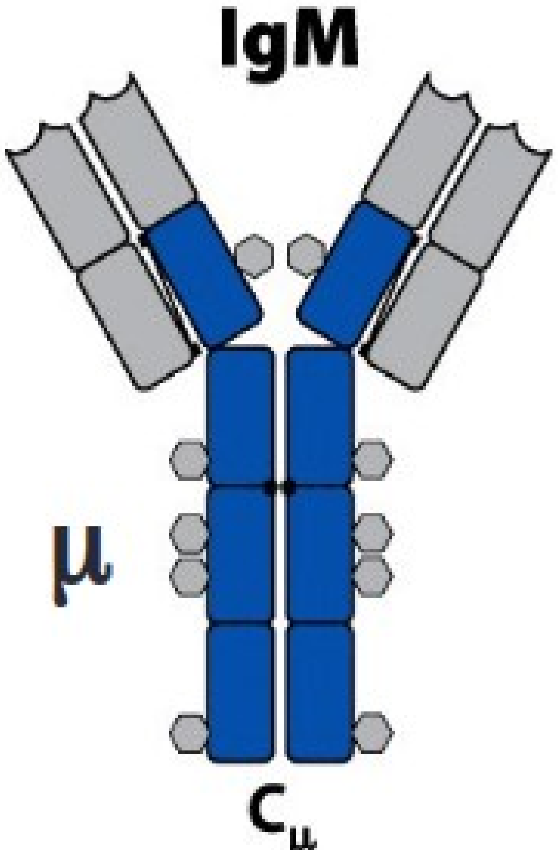


| | IgG | IgM |
|---|---|---|
| **Concentration التركيز**<br>**(of total Ab concentration}**<br>**من المجموع الكلي لتركيزAb** | 75% (most abundant)<br>**اكثر وفرة** | 10% |

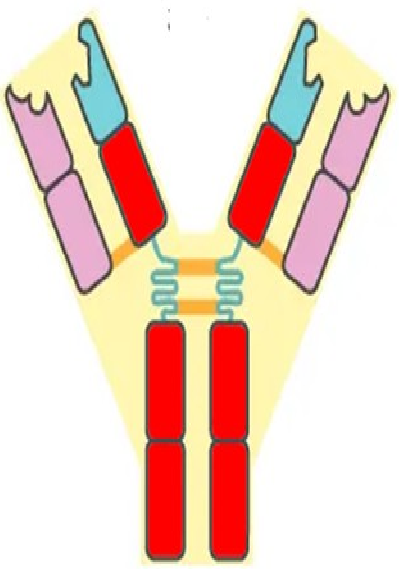


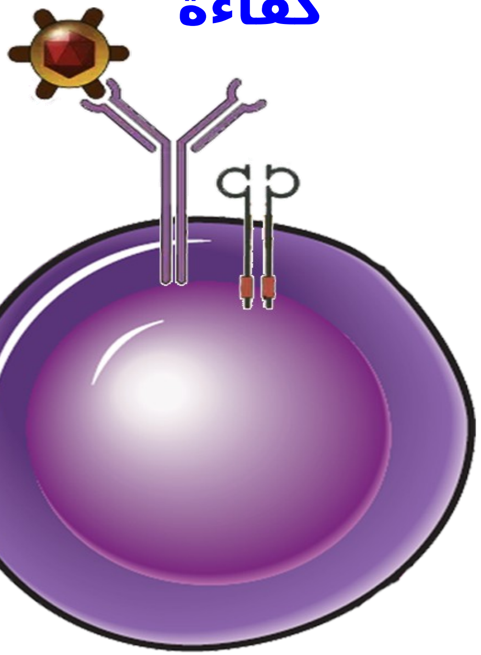
| | IgG | IgM |
|---|---|---|
| Structure | Heavy chain | |
| | γ chain | μ chain |

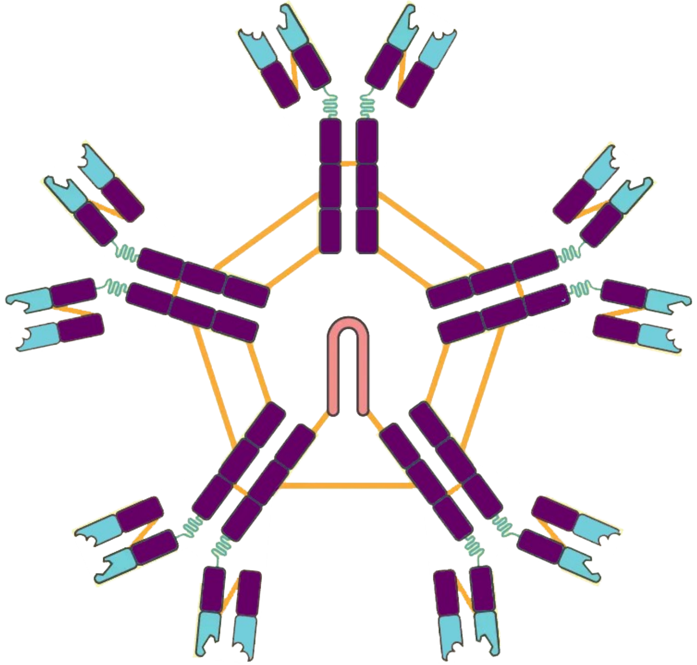




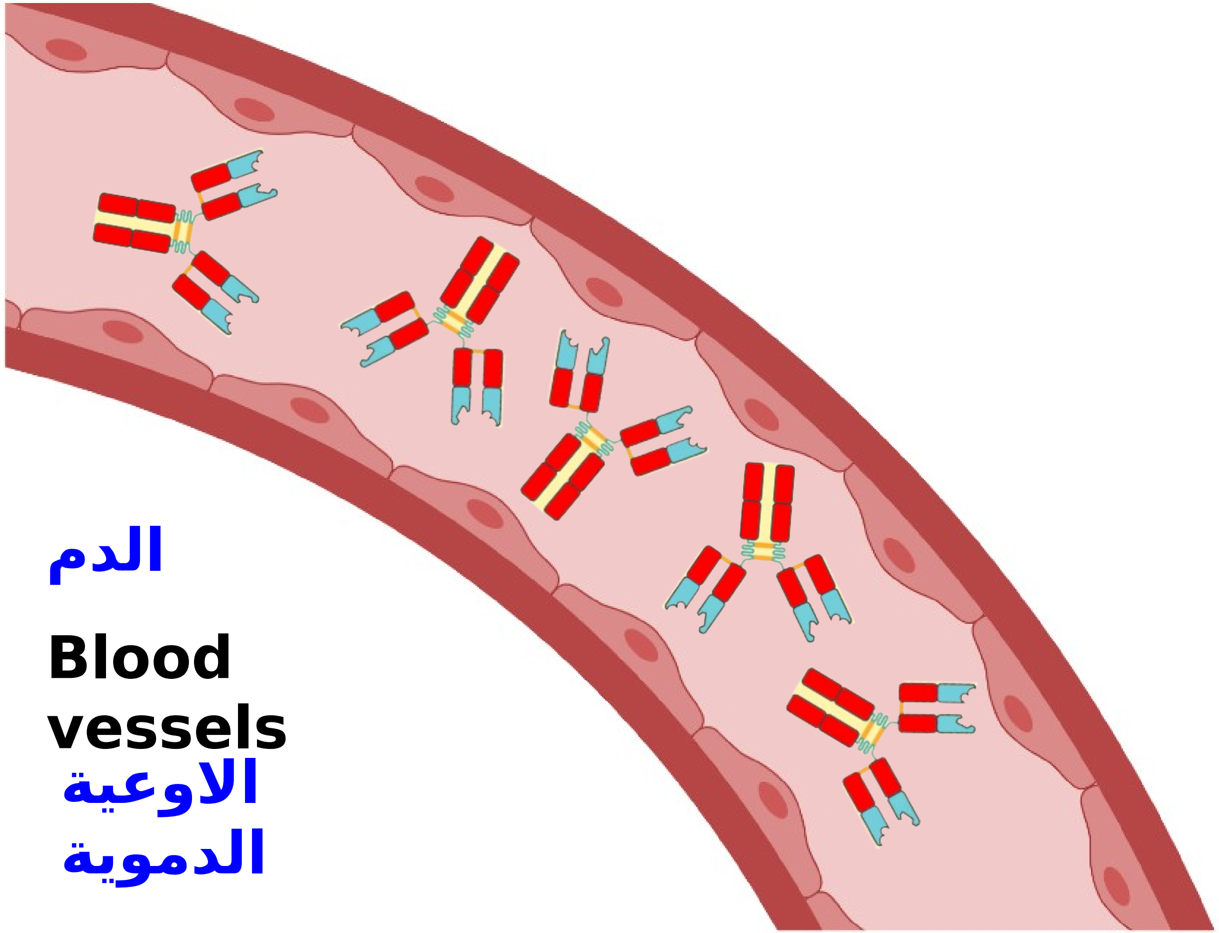
| | IgG | IgM |
|---|---|---|
| **Structure** | الأشكال. الجزيئية | Molecular forms & Molecular weight |
| | Monomer ➜<br>2 Ag binding sites<br>valency التكافؤ | 1) Monomer (membrane bound) : BCR<br>2) Pentamer (serum form): 5 monomer joined by<br>. a) Disulfide bonds b) J chain: Links 2 of the Fc<br>➥ Highest MW<br>➥ Highest valency : 10 Ag binding sites **5x2**<br>➥ Most efficient in complement activation الاكثر كفاءة |







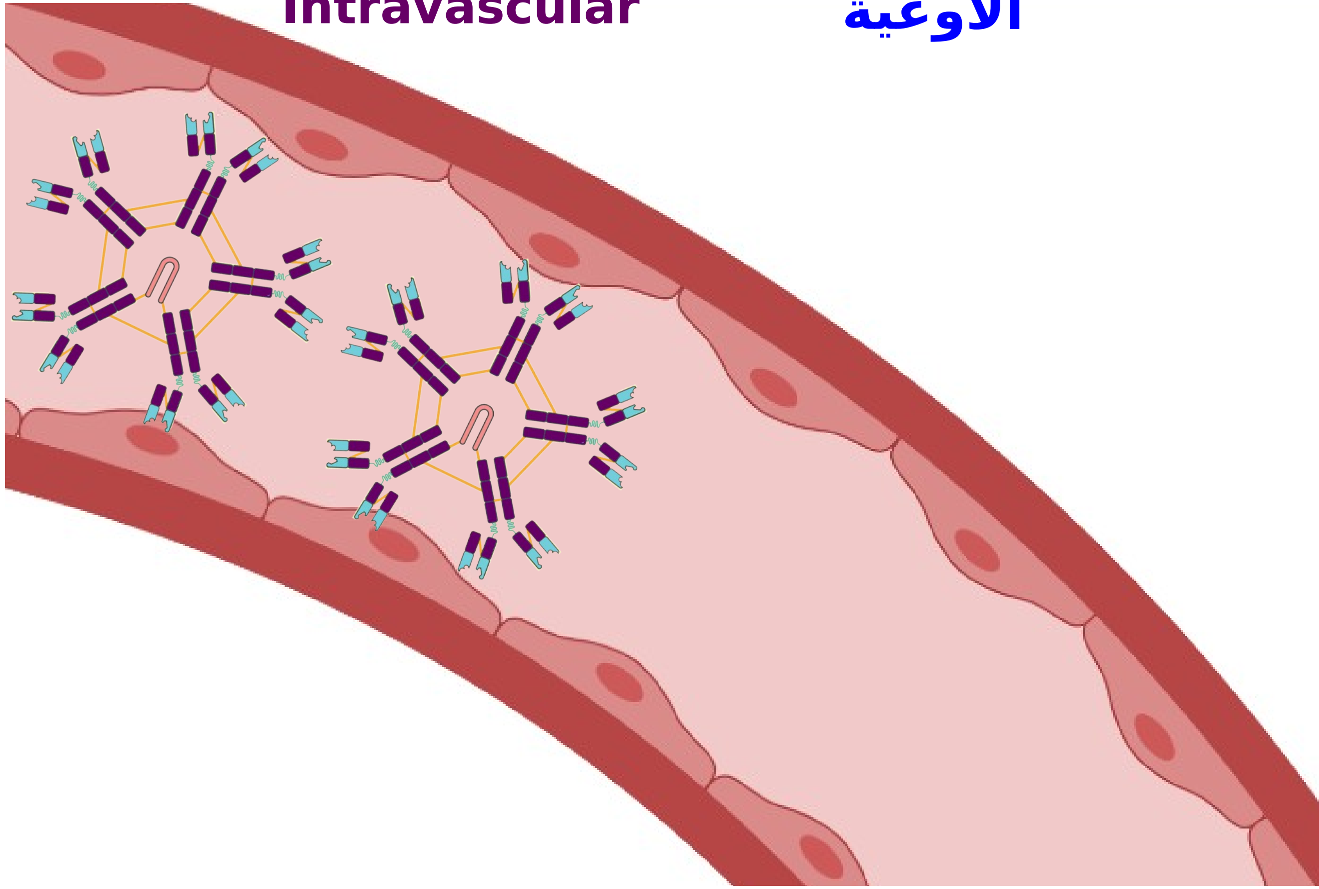
| | IgG | IgM |
|---|---|---|
| Distribution<br>التوزيع داخل الجسم | ينفذ بسهولة خارج الاوعية<br>Diffuses easily extravascular | لا ينفذ جيدا لان وزنها الجزيئي كبير<br>Doesn’t diffuse well (due to HMW) →<br>Mostly Intravascular<br>غالبا داخل الأوعية |



الدم

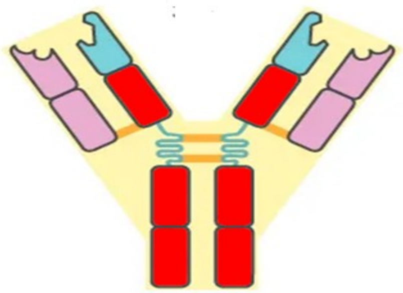
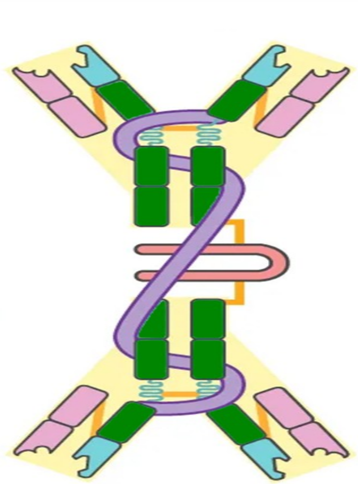
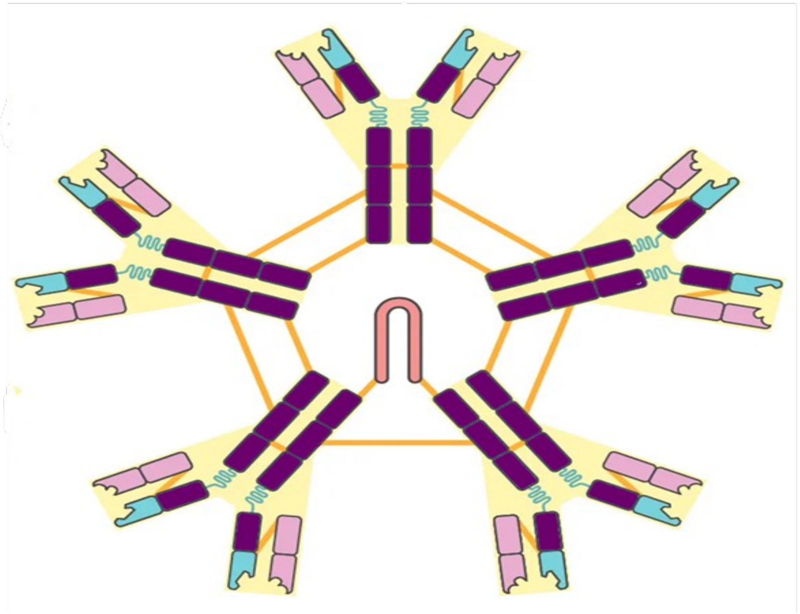
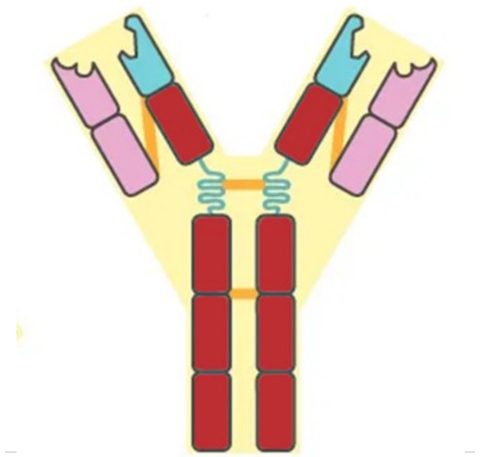
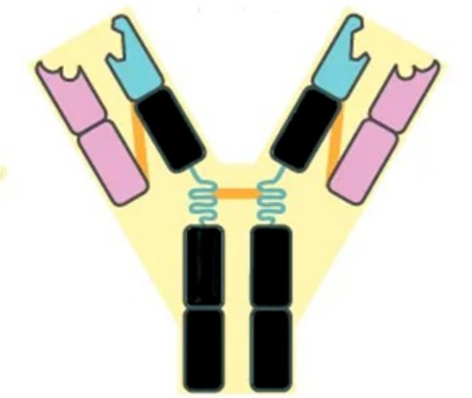
**Blood vessels**

الاوعية الدموية



# Constant region of Heavy chain

The 5 classes differ in functions

- Fc fragment differs in the 5 isotypes (classes)

➥The 5 classes have different biological functions

كل نوع لما يمسك في نسخة من ميكروب

حيعمل وظيفة مختلفة

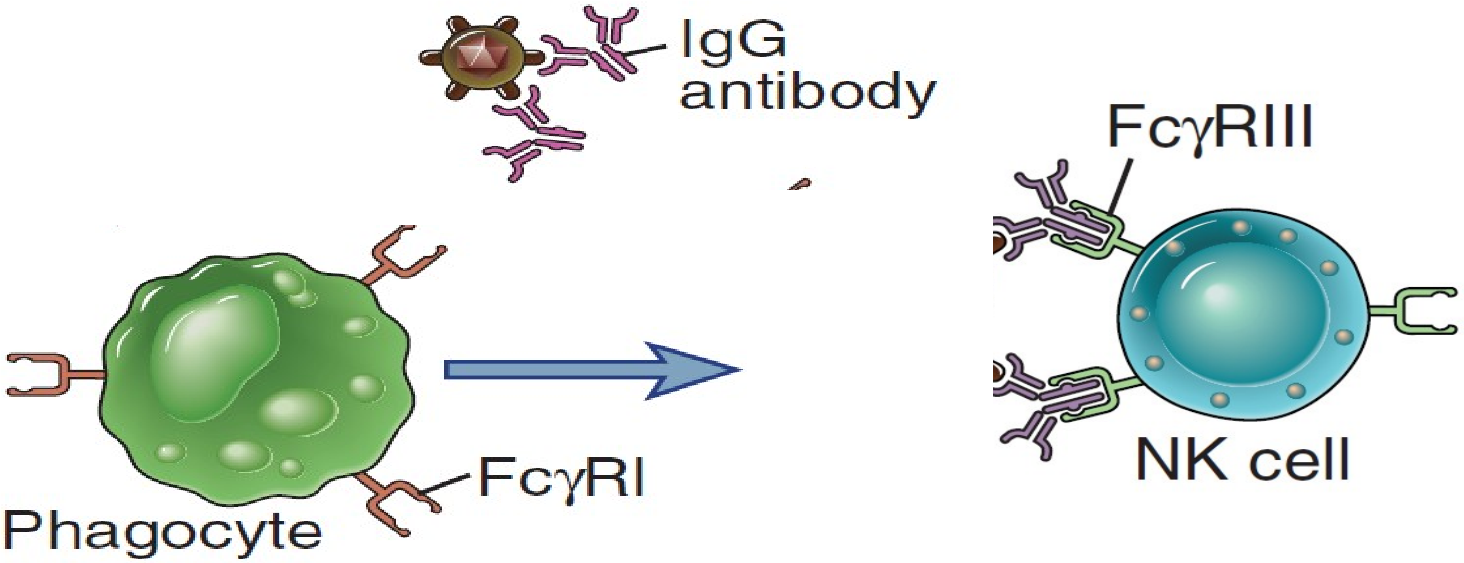
The plasma cell of each B cell clone must produce

the 5 classes of Abs against its specific Ag

كل نسيلة من B

يجب ان تنتج 5 انواع من Ab

| مسك الخلايا | IgG | IgM |
|---|---|---|
| Binding to immune cells | **Binds to Fc γ R on phagocytes & NK cells**<br>**حبيب الملايين** | NO<br>**منبوز** |



# Functions of Igs

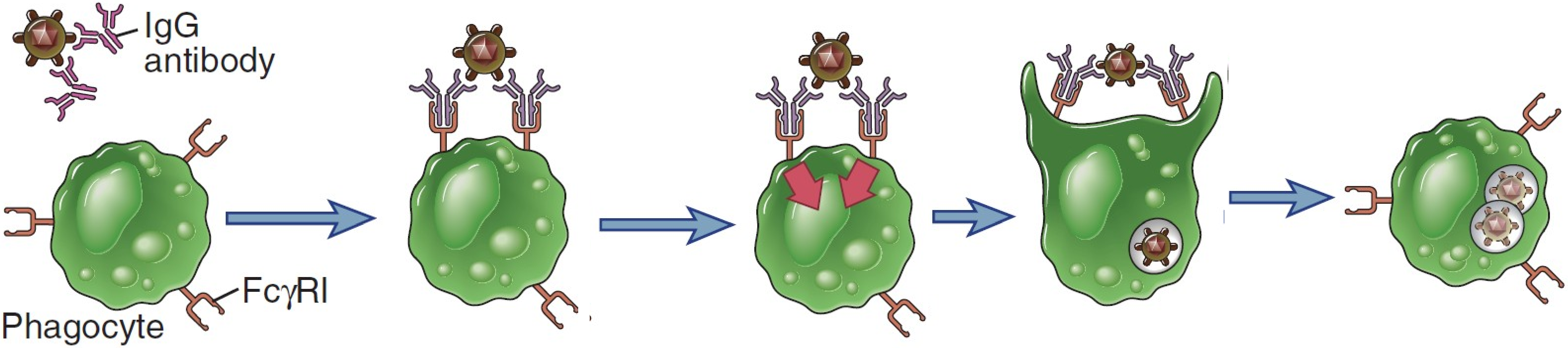
مرتبطين بخلايا

**Only by IgG**

- Opsonization
- ADCC
- Activation of complement
- Neutralization

بتاع كله

| | **IgG** | **IgM** |
|---|---|---|
| **Functions** | 1) Opsonization | |
| | IgG (opsonin) binds organism<br>Binds to Fcγ R on phagocytes (MQ & neutrophils)<br>↓<br>Facilitates ingestion يسهل الابتلاع | NO |

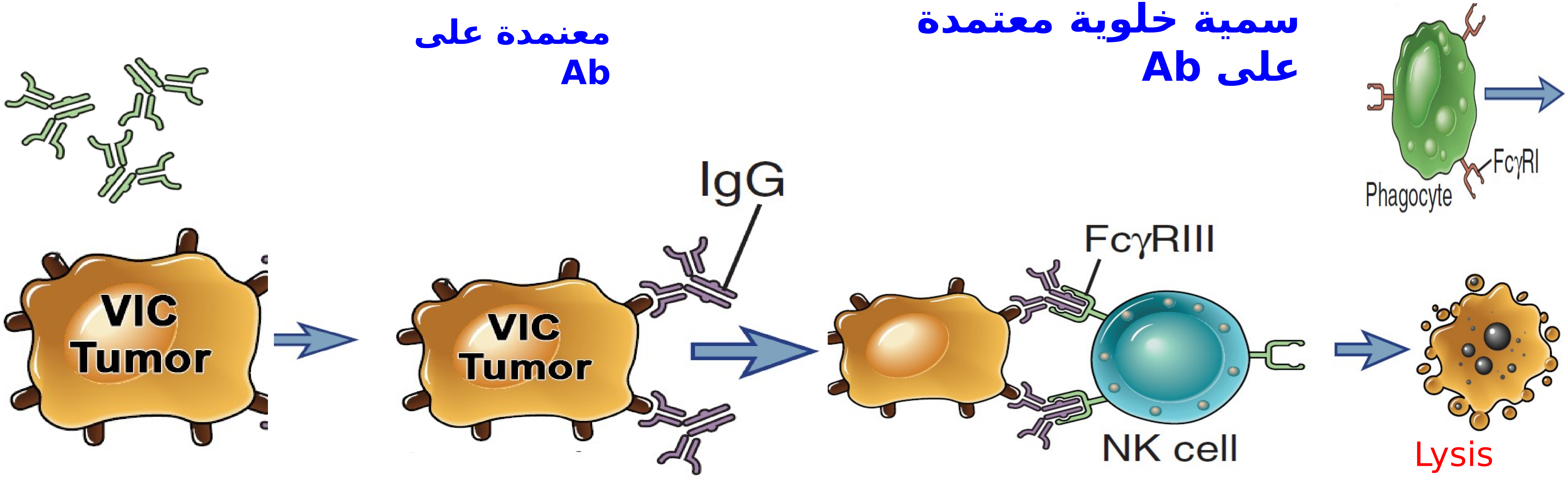


| | IgG | IgM |
|---|---|---|
| **Functions** | 2) ADCC (Ab dependent cellular cytotoxicity) | |
| | IgG binds target cells e,g virally infected cells<br>↓<br>Binds to Fcγ R on NK or phagocytes<br>↓<br>Lysis of targets **bound by Abs** | NO |

**موت الاهداف الممسوكة بال Ab**

**سمية خلوية معتمدة على Ab**

**معتمدة على Ab**



# Effector functions of Igs

- Opsonization :Phagocytes

مرتبطين بخلايا

**Only by IgG**

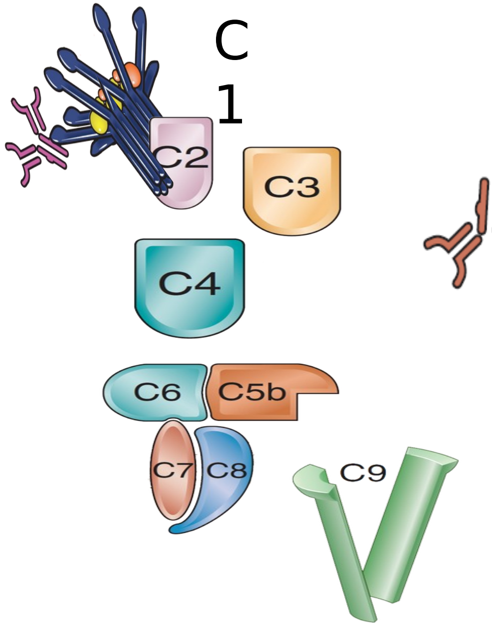
- ADCC: NK& Phagocytes

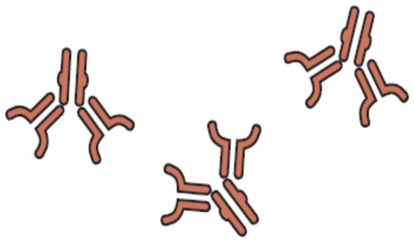
- Activation of complement

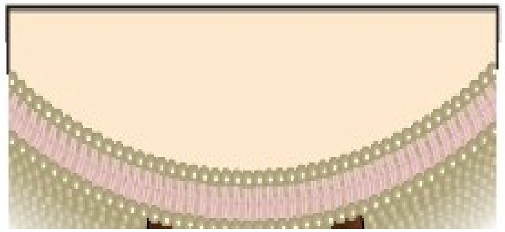
غيرمرتبطين بخلايا

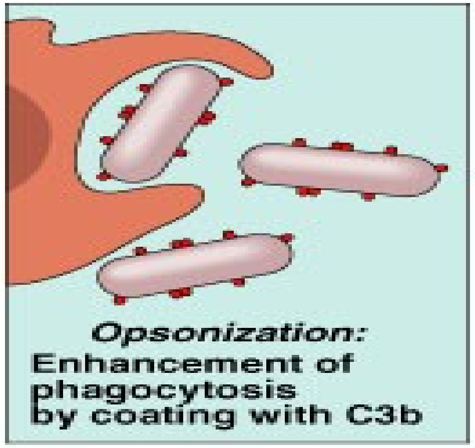
- Neutralization

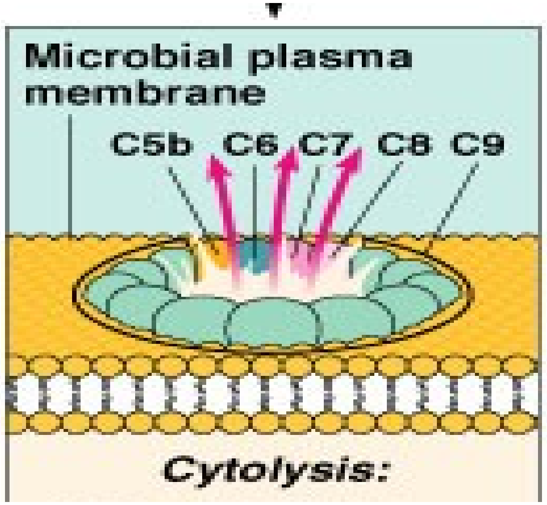
|  | IgG | IgM |
|---|---|---|
| **Effector mechanisms** | 3) Complement activation: by classical pathway | المسار الكلاسيكي |
|  | Yes<br>opsonization & cell lysis | Most efficient<br>الاكثر كفاءة |

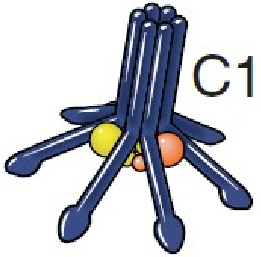


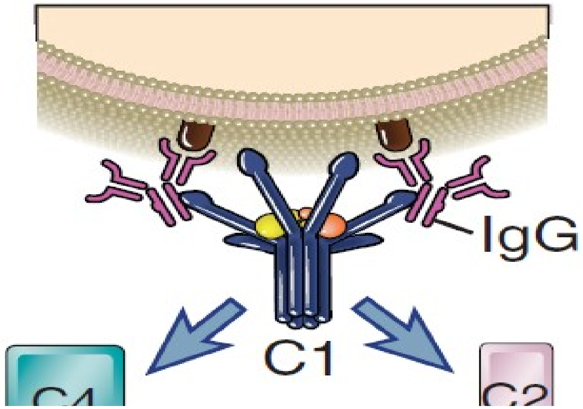





Opsonization:
Enhancement of phagocytosis by coating with C3b

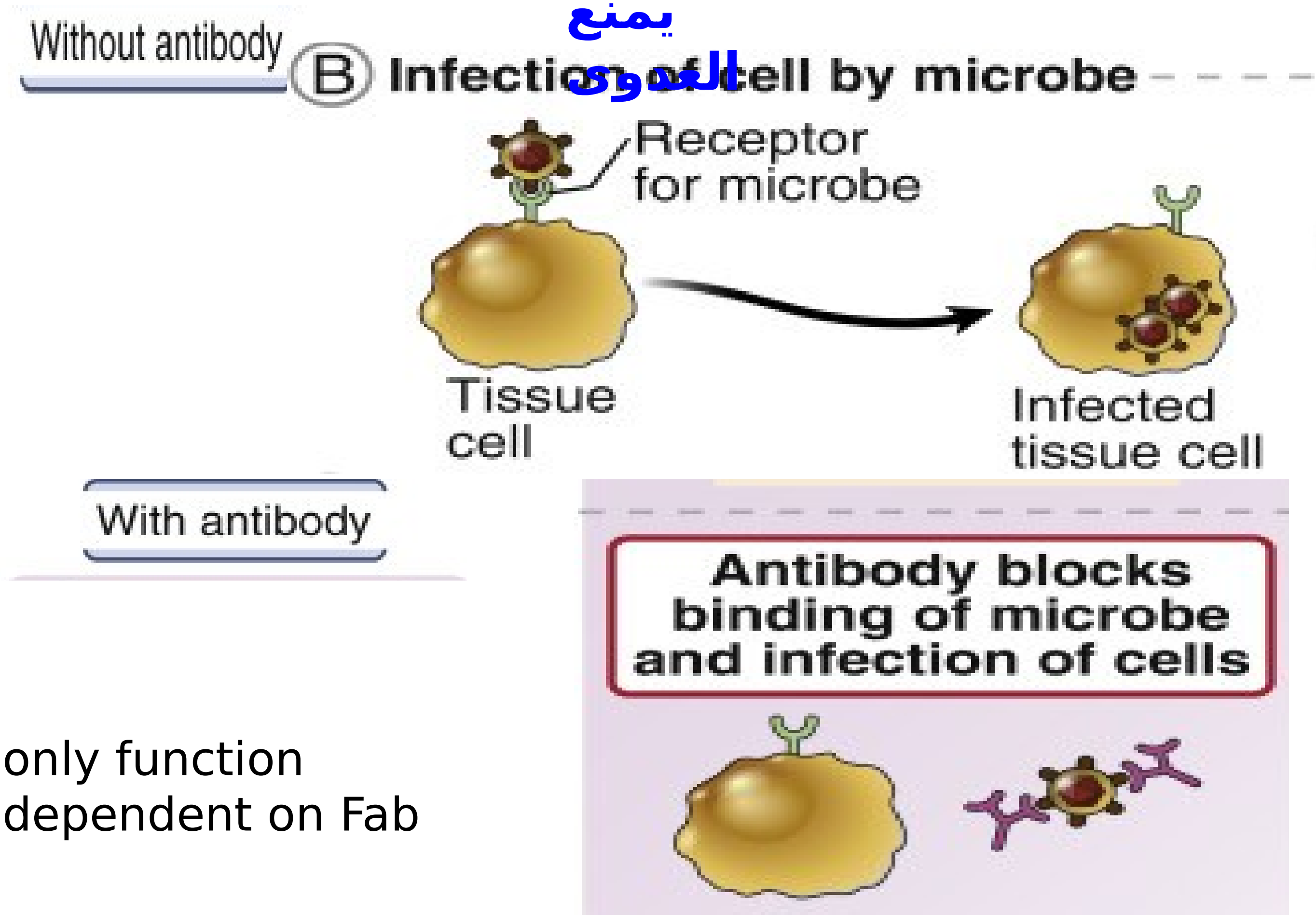




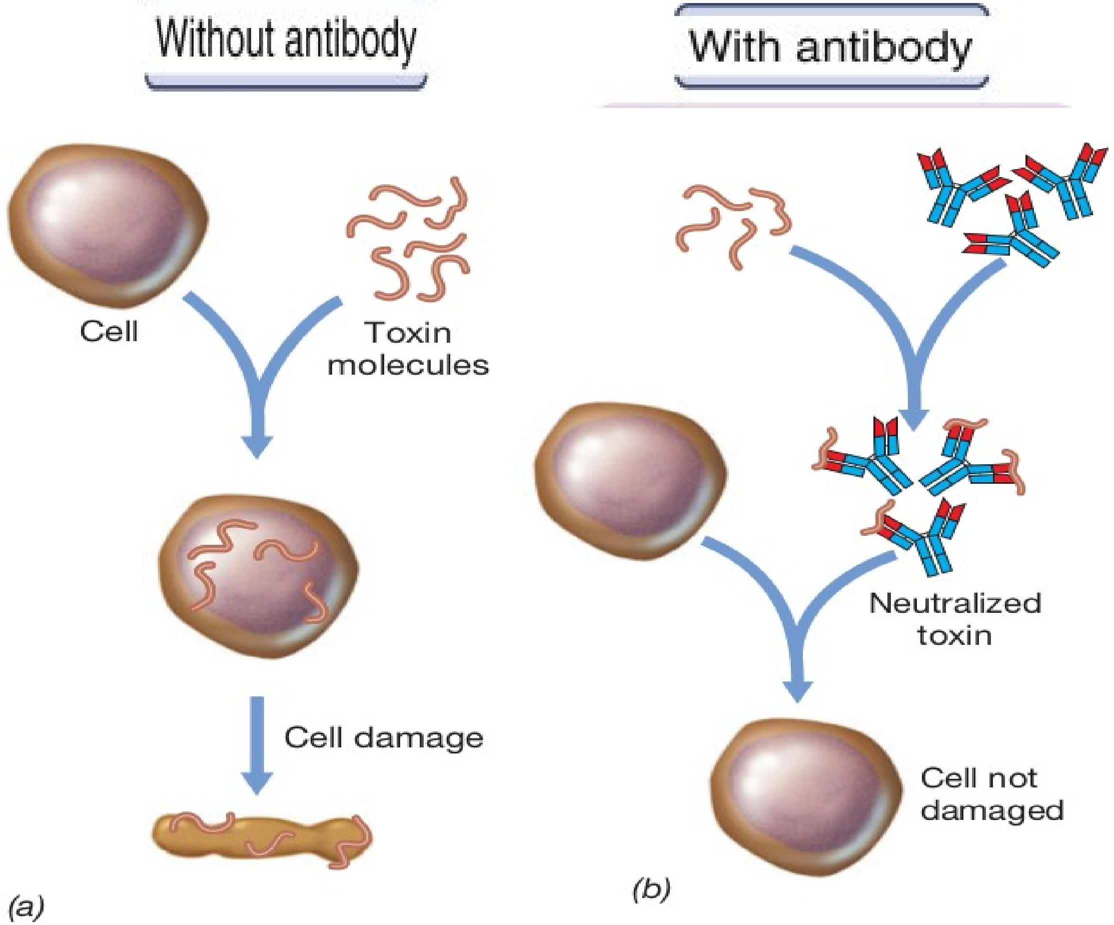


| | IgG | IgM |
|---|---|---|
| **Functions** | 4) Neutralization معادلة تمنعه من الوصول الى هدفه<br>IgG prevents binding of viruses & toxins to their target cells<br>➥inhibits infectivity of viruses & blocks action of toxin تمنع عمله | Yes |

يمنع العدوى


Without antibody
B Infection of cell by microbe
Receptor for microbe
Tissue cell
Infected tissue cell
With antibody
Antibody blocks binding of microbe and infection of cells

only function dependent on Fab



# Effector functions of Igs

مرتبطين بخلايا

- Opsonization :Phagocytes

**Only by IgG**

- ADCC: NK& Phagocytes

غيرمرتبطين بخلايا

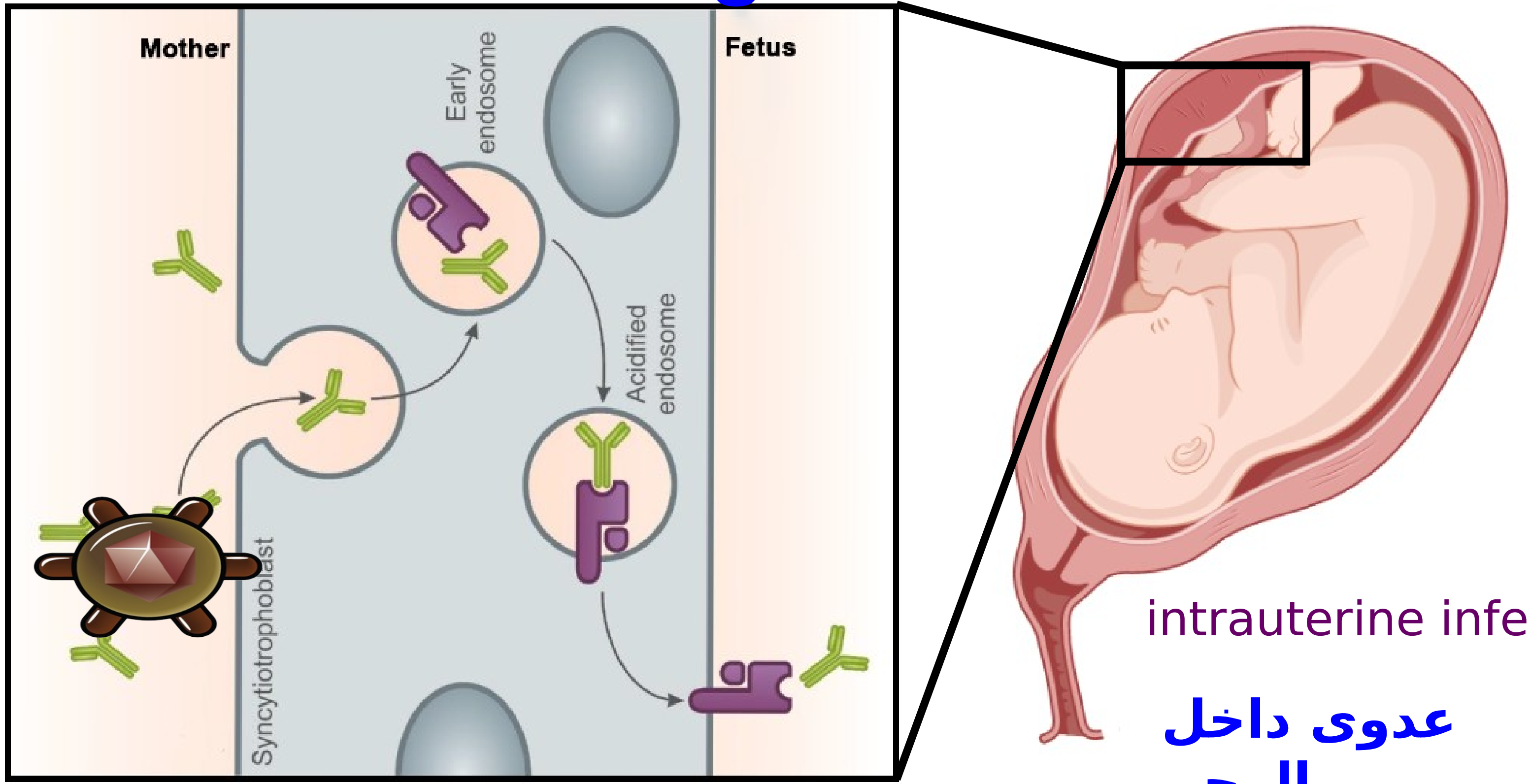
- Activation of complement

Most efficient

مرتبطين بالوزن الجزيئي

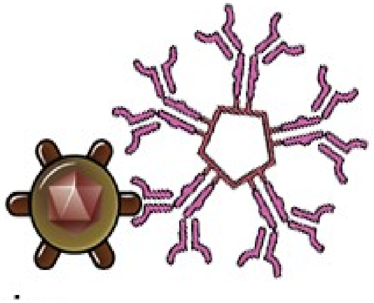
- Neutralization

| | IgG | IgM |
| --- | --- | --- |
| | Placental passage عبور المشيمة | |
| **Other properties** | Only Ig that crosses the placenta<br>↓<br>Immunity to fetus<br>الجنين | **NO,** but is the 1st Ig synthesized by fetus<br>↓<br>Indicates intrauterine infection<br>يشير الى<br>if ↑ in neonates<br>حديث الولادة |

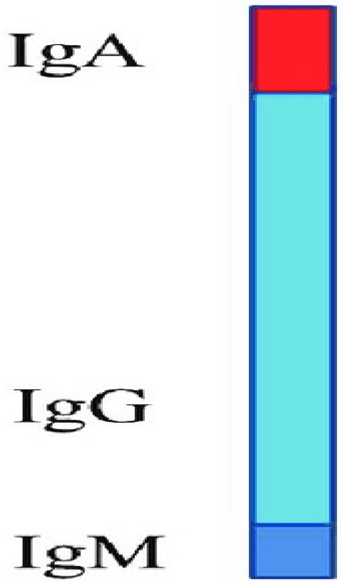


intrauterine infection

عدوى داخل الرحم



# Ig A



**Concentration**

15% of total serum Igs

وظيفته مش علينا

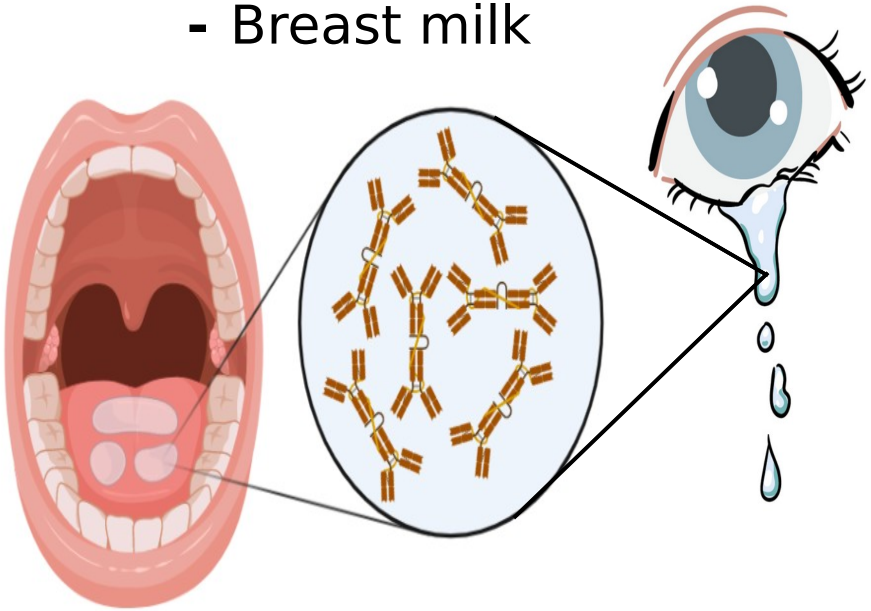
**Site & Characters**

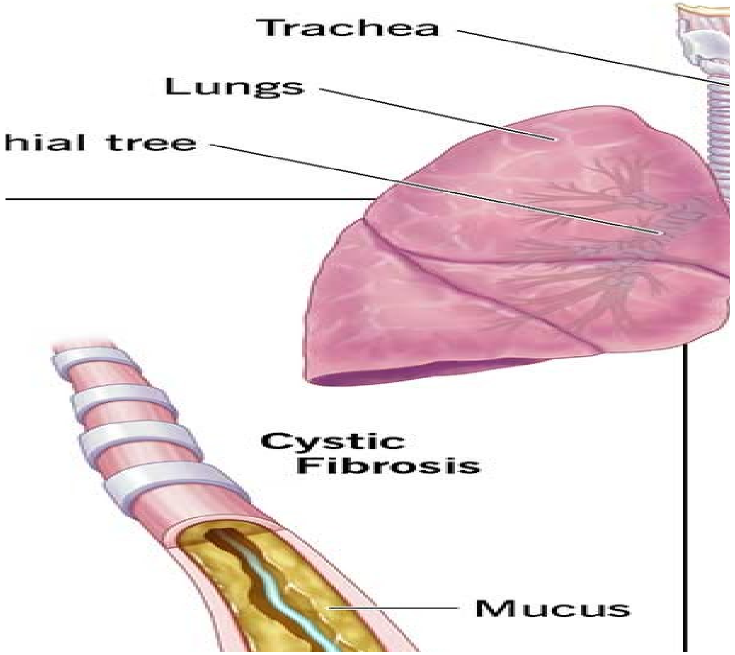
المكان والخصائص

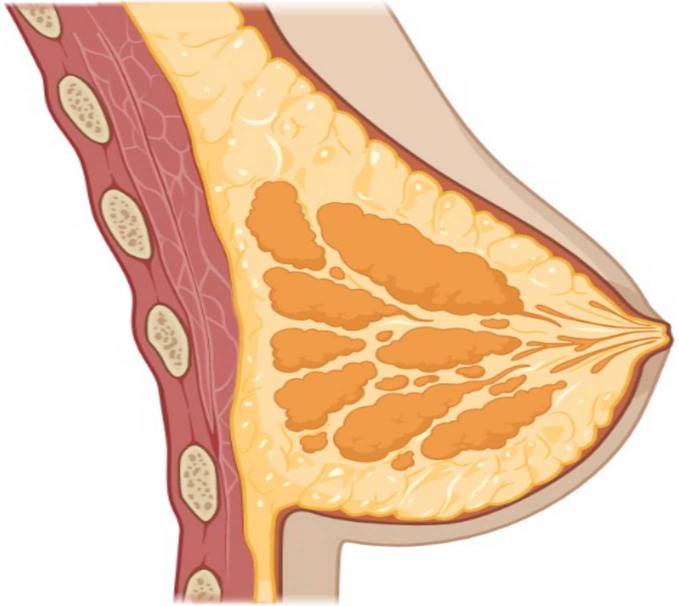
Secretory IgA : Main Ab in secretions

الرئيسي في الافرازات

- Saliva & tears
- Mucus of RT & GIT المخاط
- Breast milk

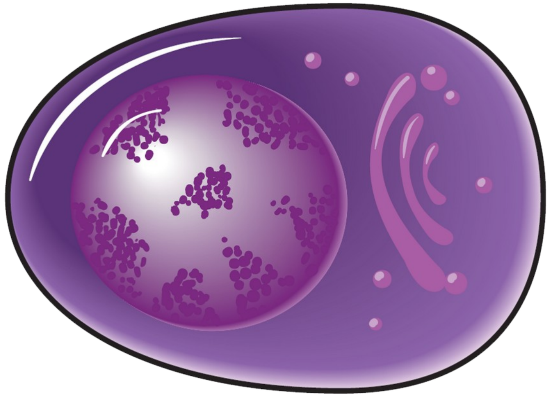


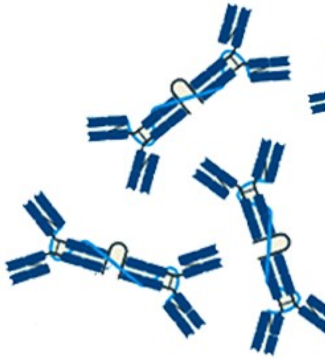


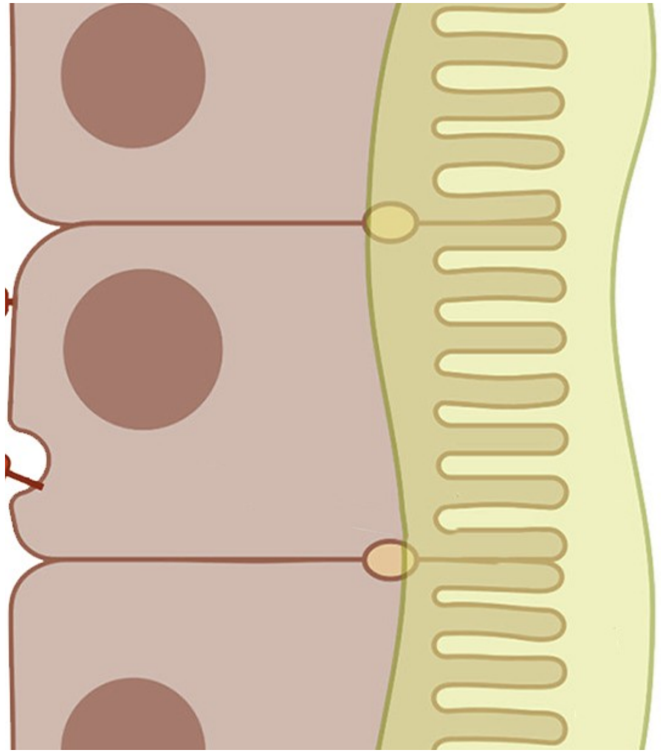


# Ig A

Synthesized by submucosal plasma cells







secretions

**Submucosa**

ما تحت

**Epithelium**

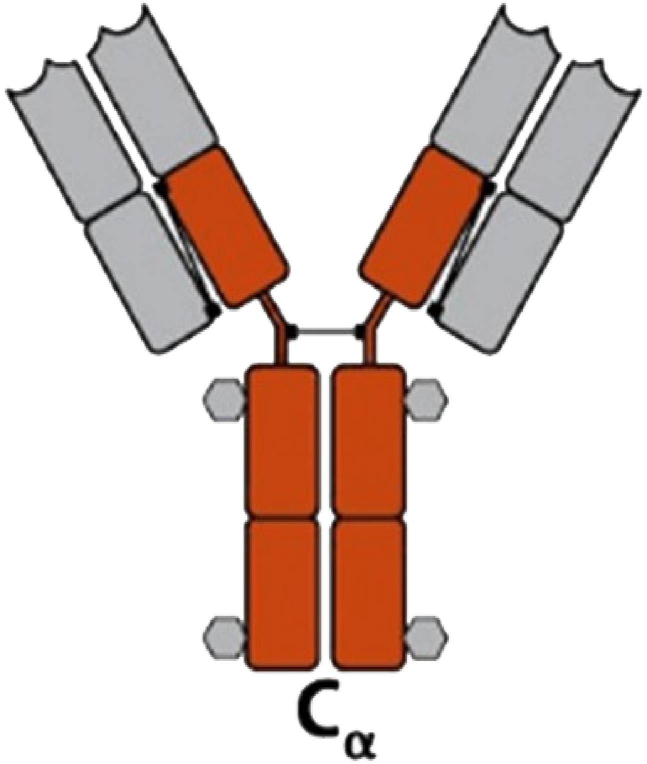
الغشاء المخاطي

الافرازات

# Ig A

## Structure

- Heavy chain: **α** chain



Structure

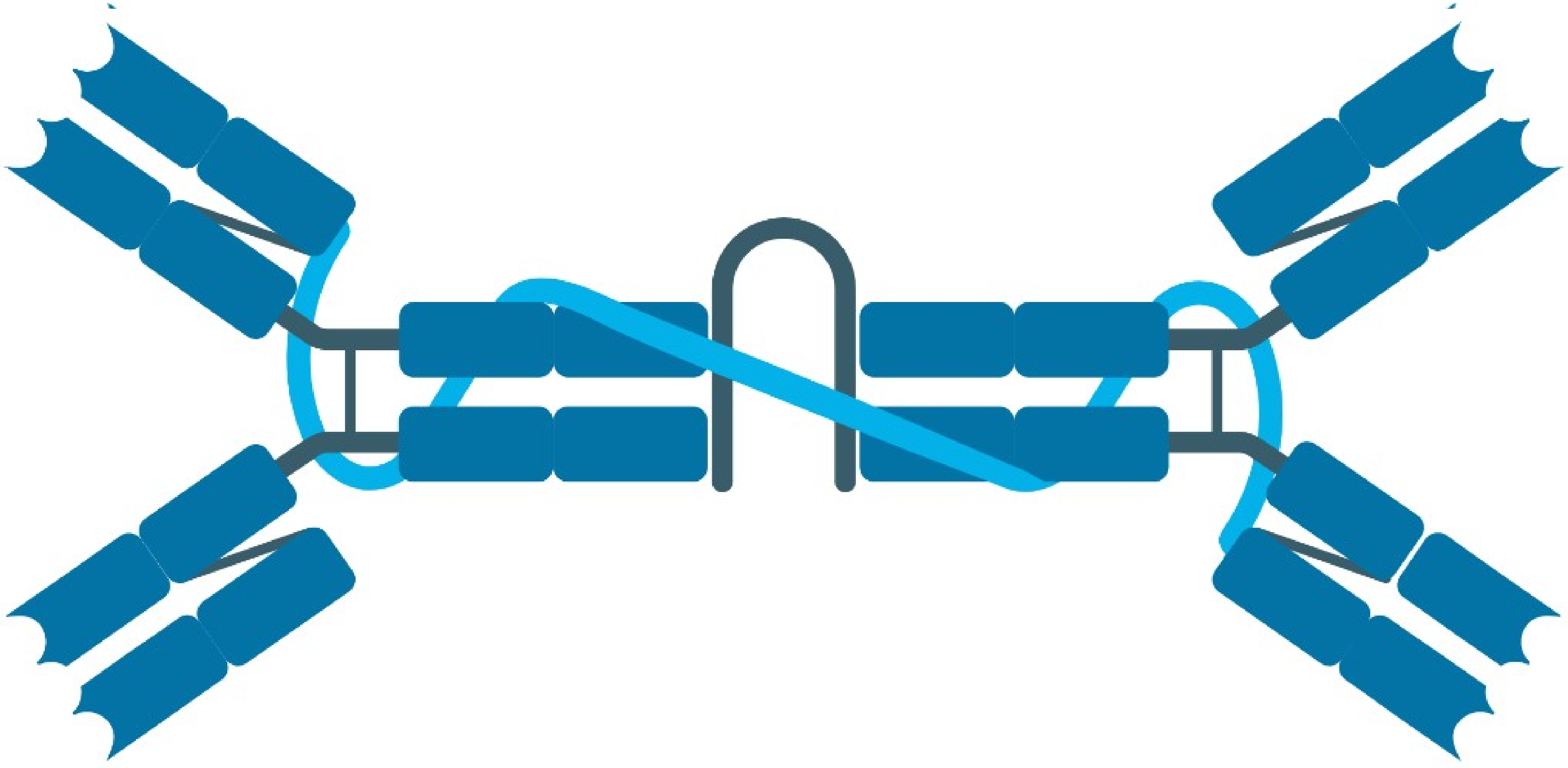
## - Molecular forms:

**الأشكال.**
**الجزيئية**

Secretory IgA is a dimer:

2 monomers joined by J chain

- Secretory (S) component



**Remember**
**serum IgM**

5

**مكون**

# Functions

Local mucosal immunity

المناعة المخاطية
الموضعية

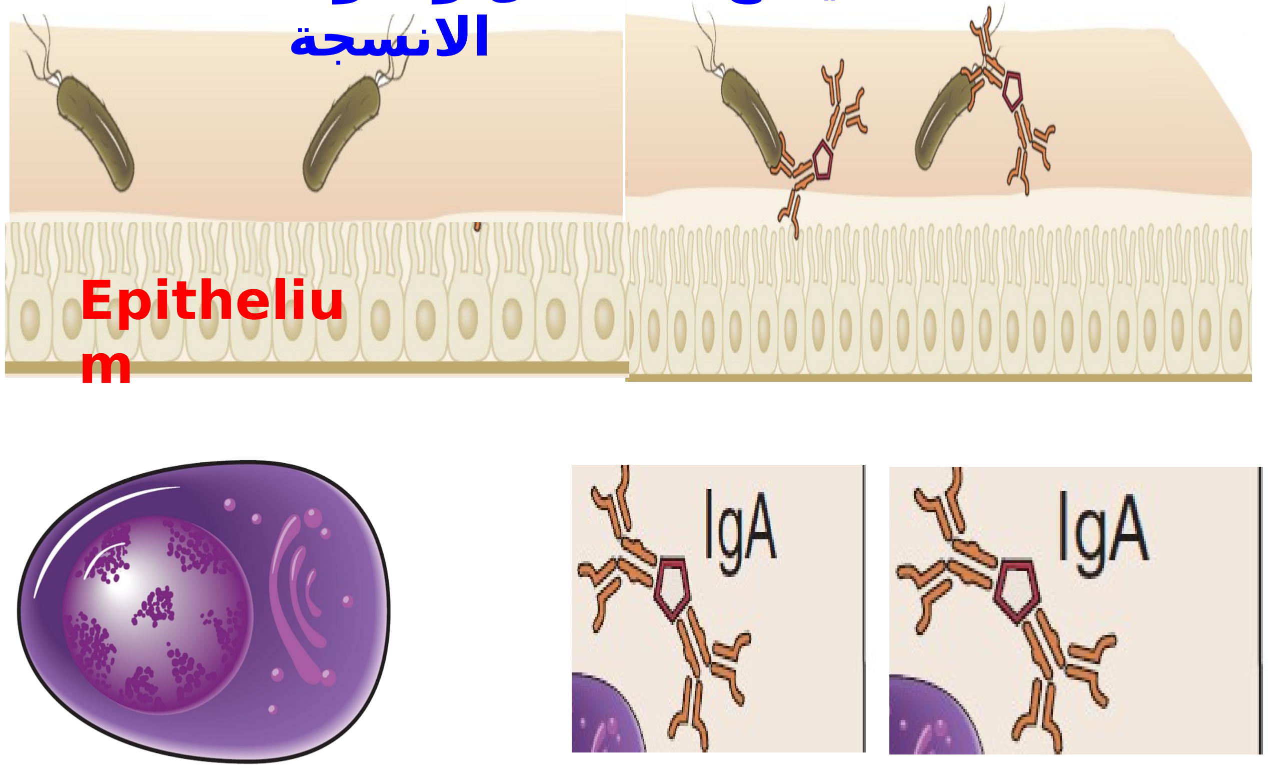
حارس بوابة الجسم

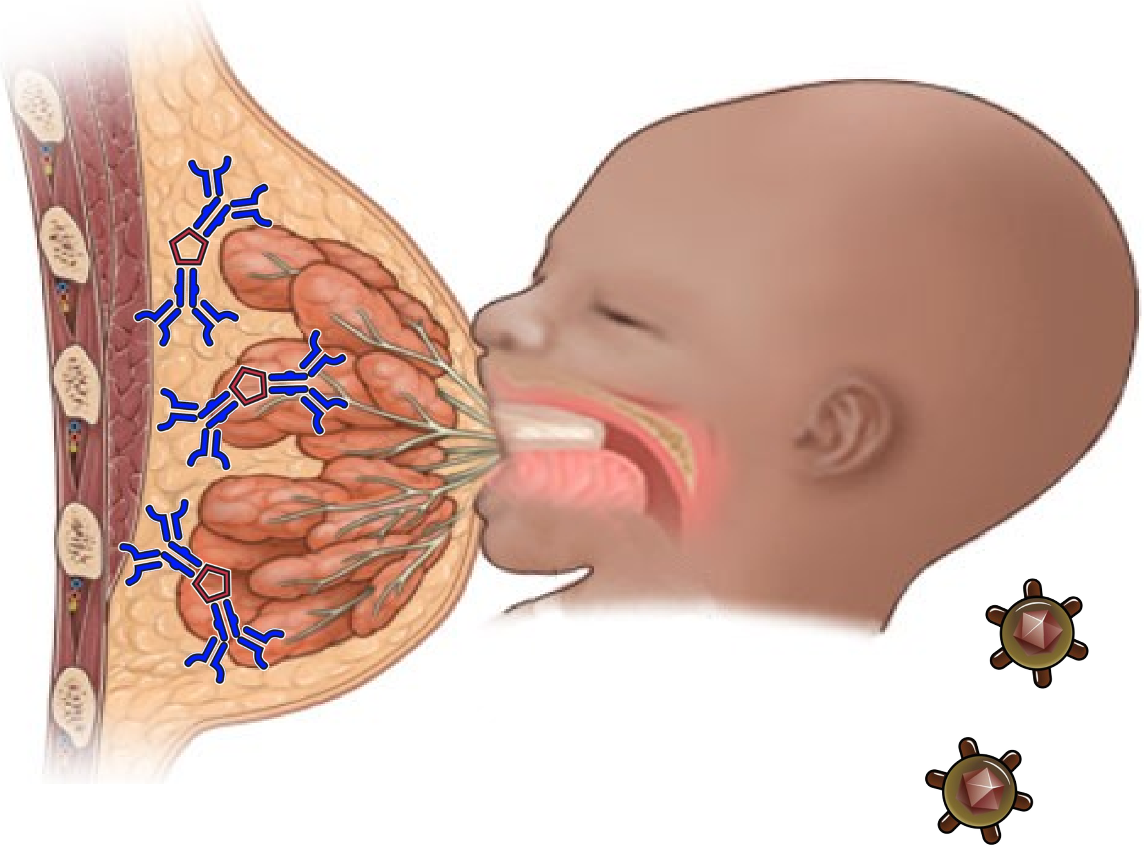
Neutralizes bacteria & viruses in mucosa
↓
Prevent their adherence & entry in tissues

يمنع الالتصاق ودخول
الانسجة

Present in milk
↓
Protects newborn from infection

المولود
حديثا

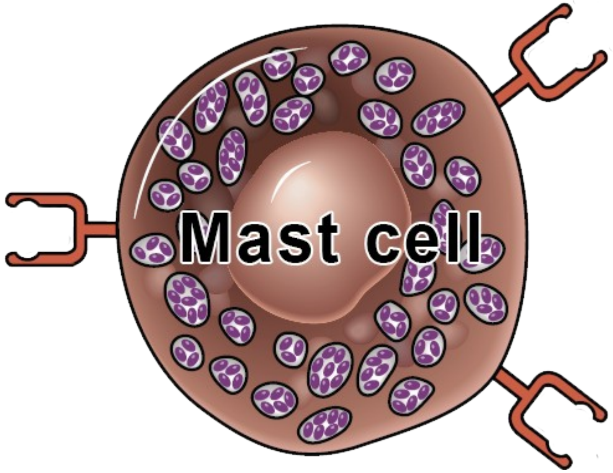


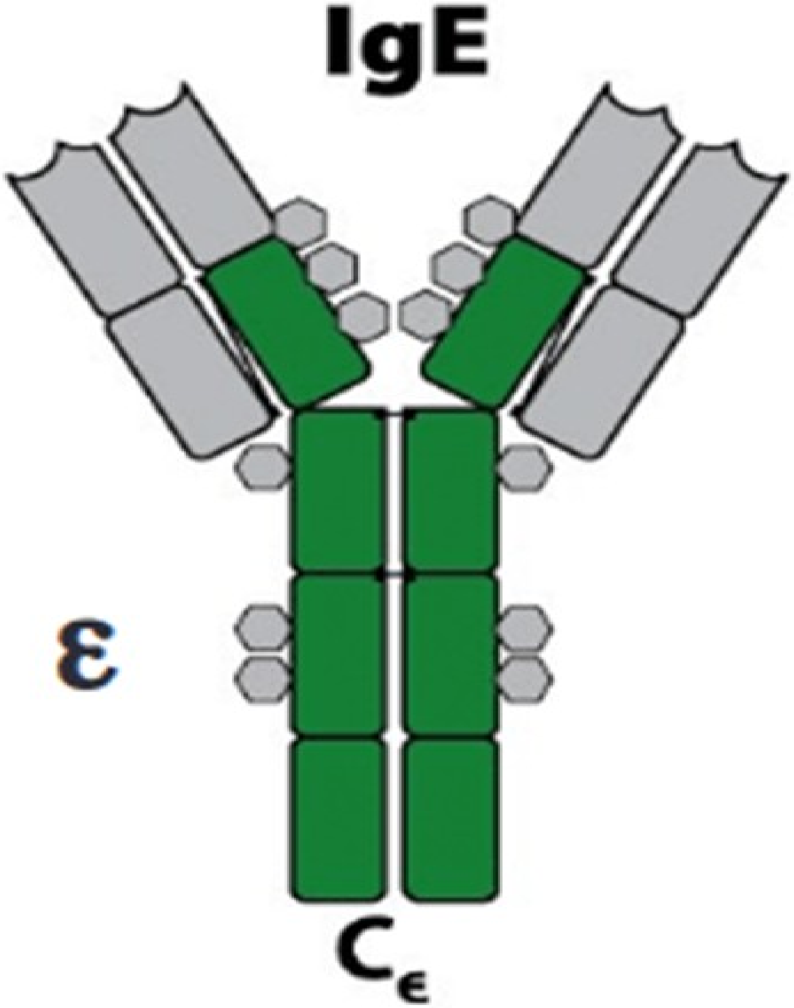


# Ig E

## Structure

- Heavy chain: ε chain





# Ig E

## Concentration

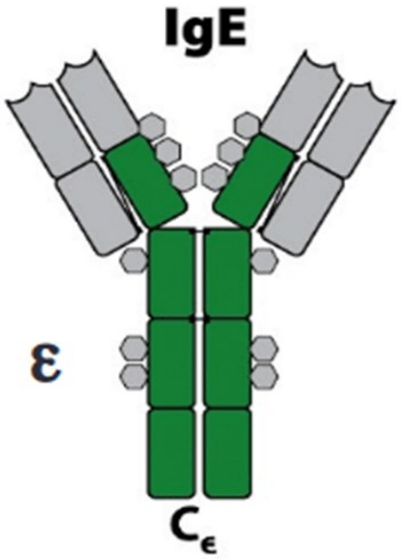
very low

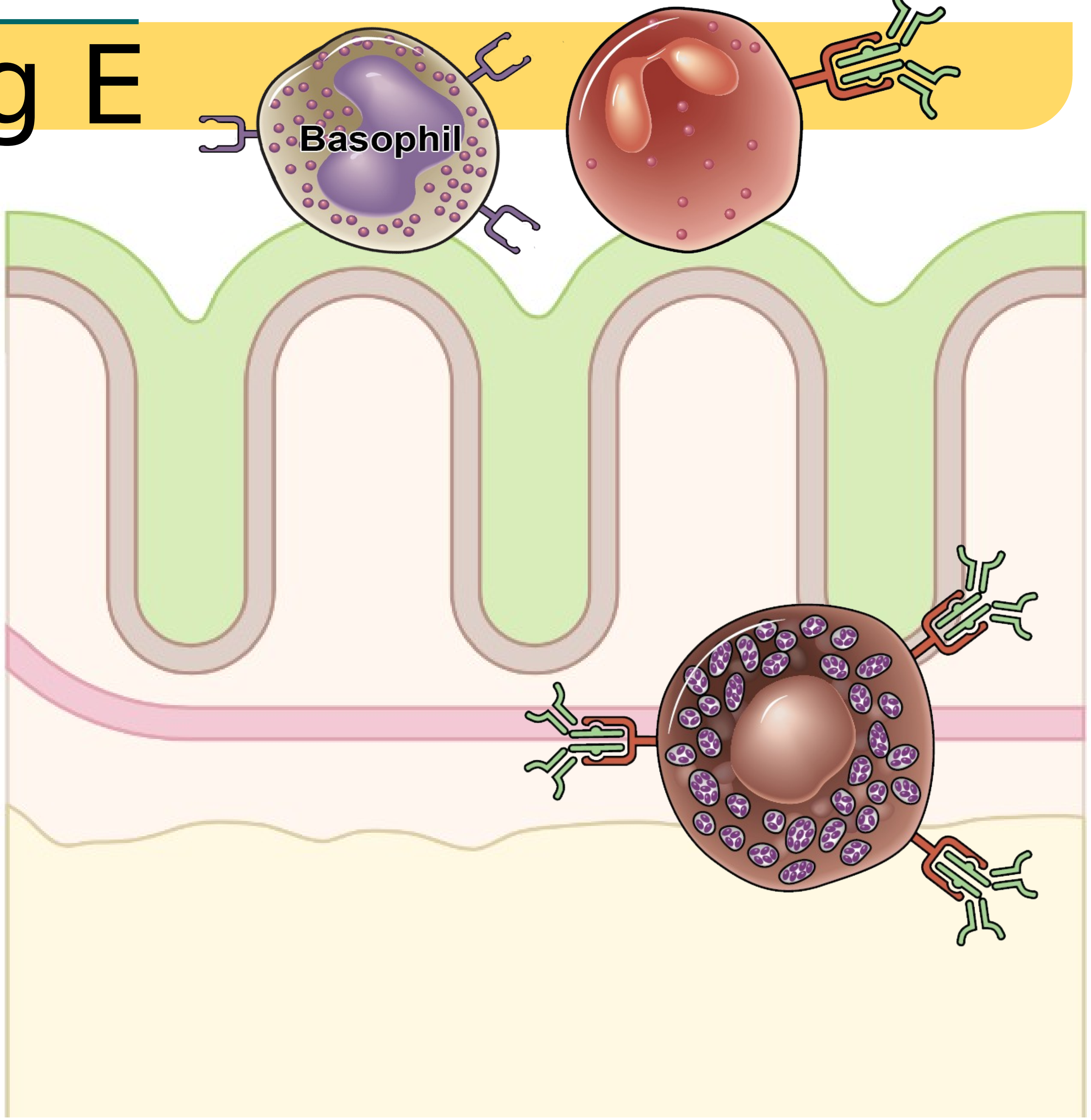
## Site & Characters

-  Mucosa
-  Bind to FcεR on
  - mast cells
  - basophils
  - eosinophil

Inflammatory cells

involved in allergy





# Ig E

## Functions

### 1) ADCC (Ab dependent cellular cytotoxicity)

سمية خلوية

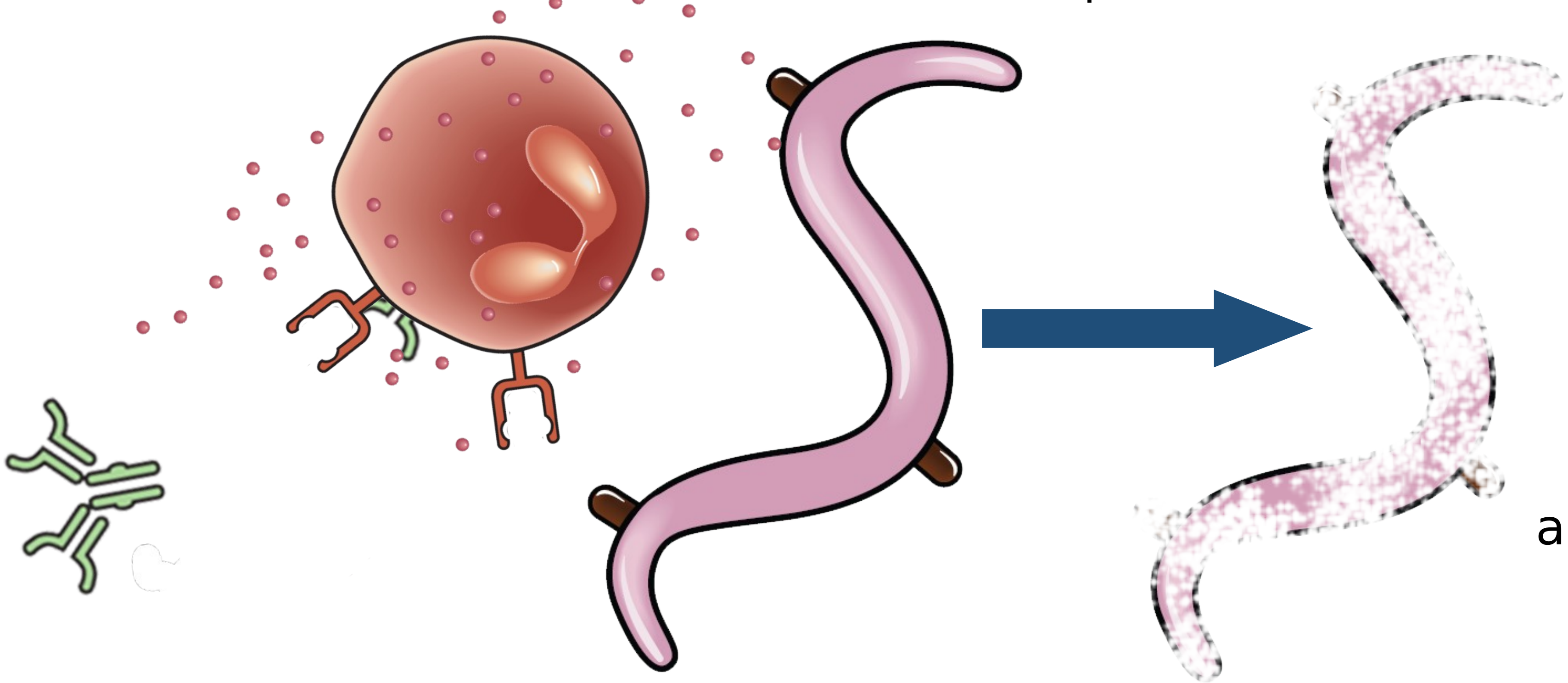
يمسك

IgE coats helminths → Binds to FcεR on eosinophils

→ releases toxic protein

→ Kill parasite (helminths)

**Remember Th2**



IgE
is the main
host defense
against parasites

دفاع العائل الرئيسي

# 2) Allergic manifestations

مظاهر الحساسية

IgE binds to FcεR on mast cells , basophils & eosinophils

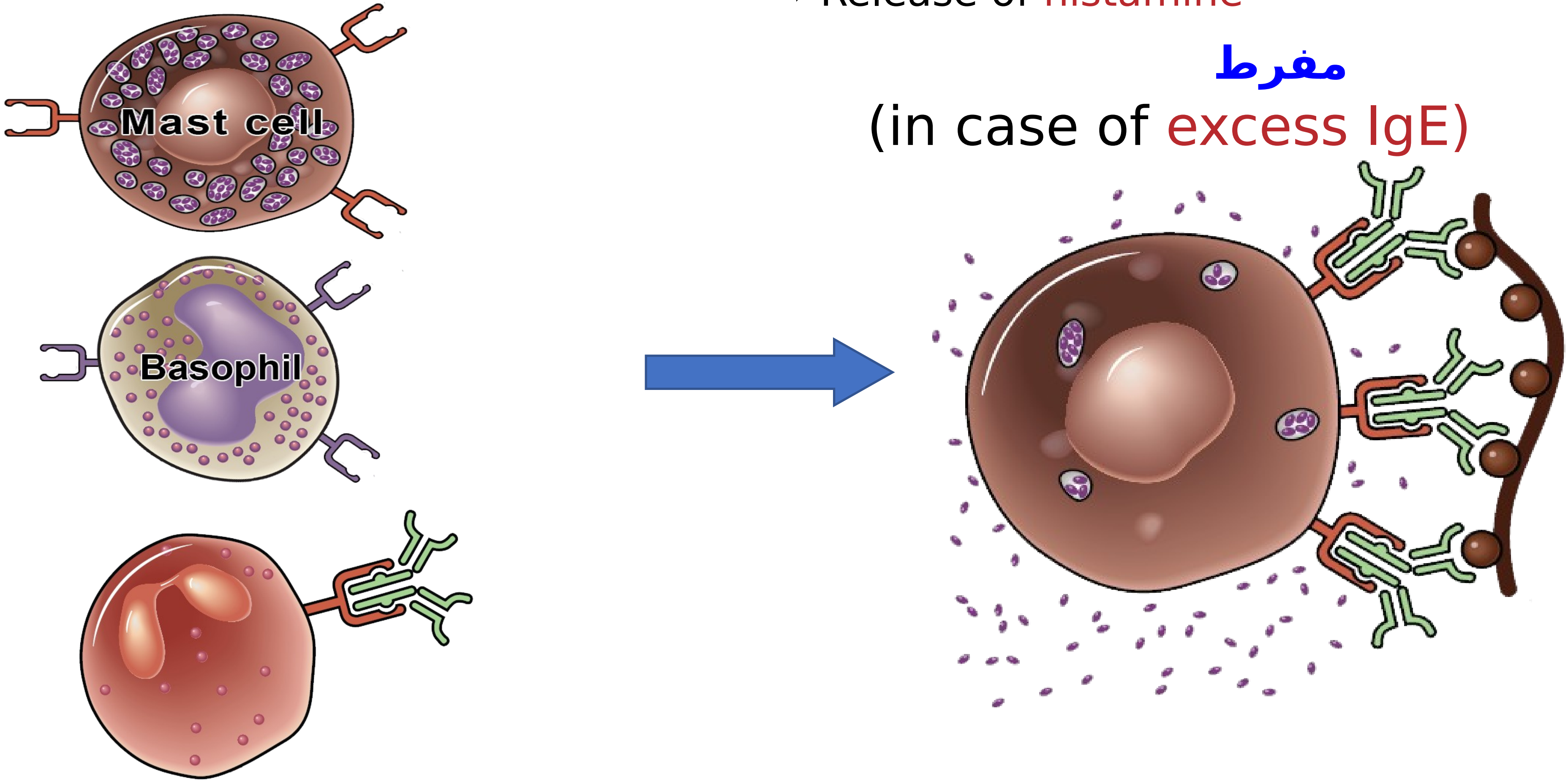
فرقعة الحبيبات

➥ Degranulation on Ag binding

➥ Release of histamine

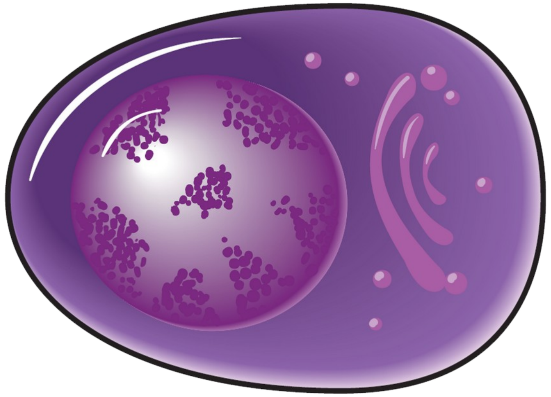
مفرط

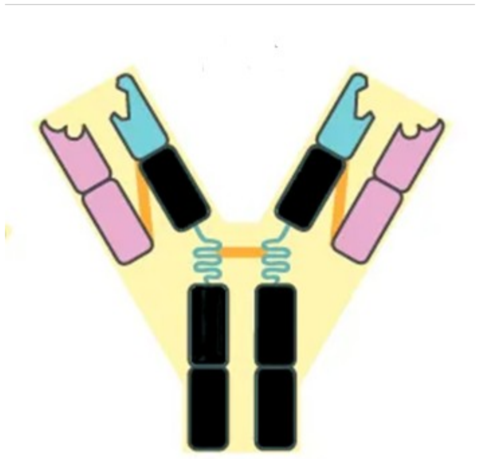
(in case of excess IgE)



# IgD

**Concentration** 0.2 % of total serum Igs





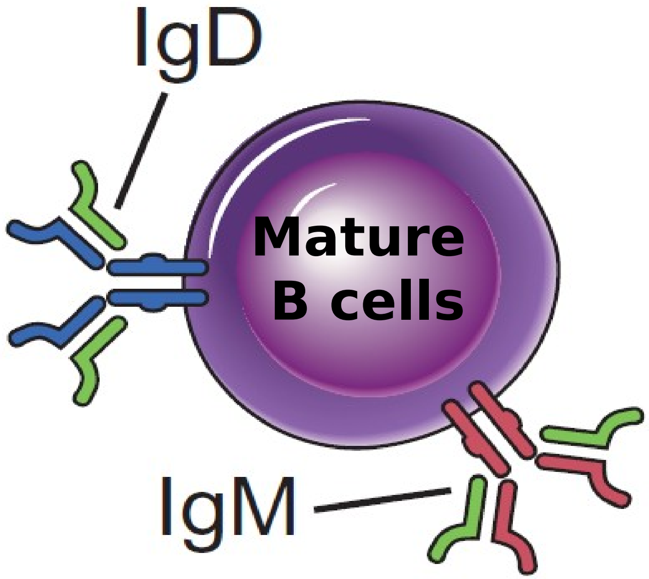
**Function**

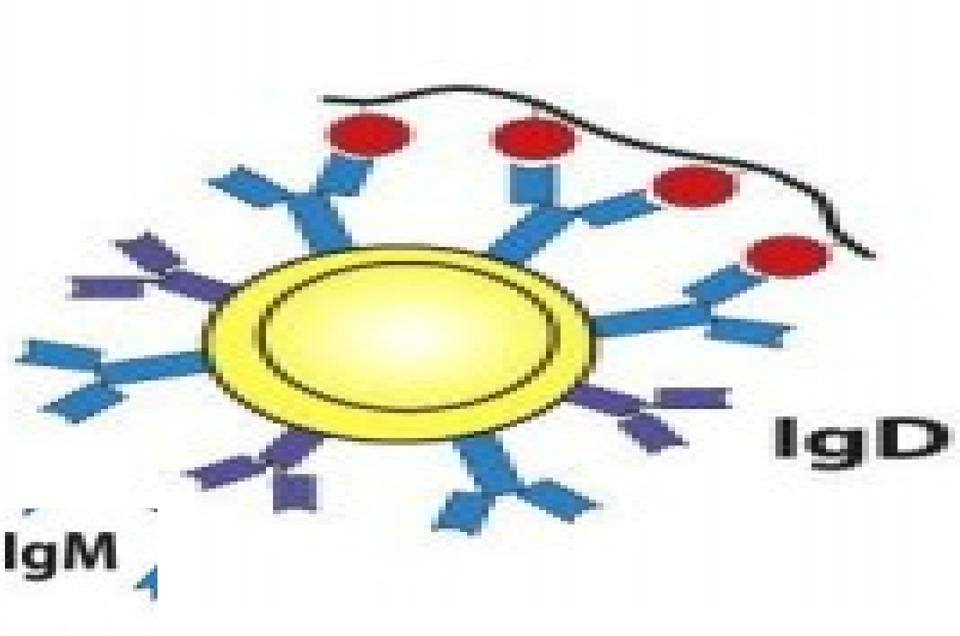
Ag receptor (BCR):

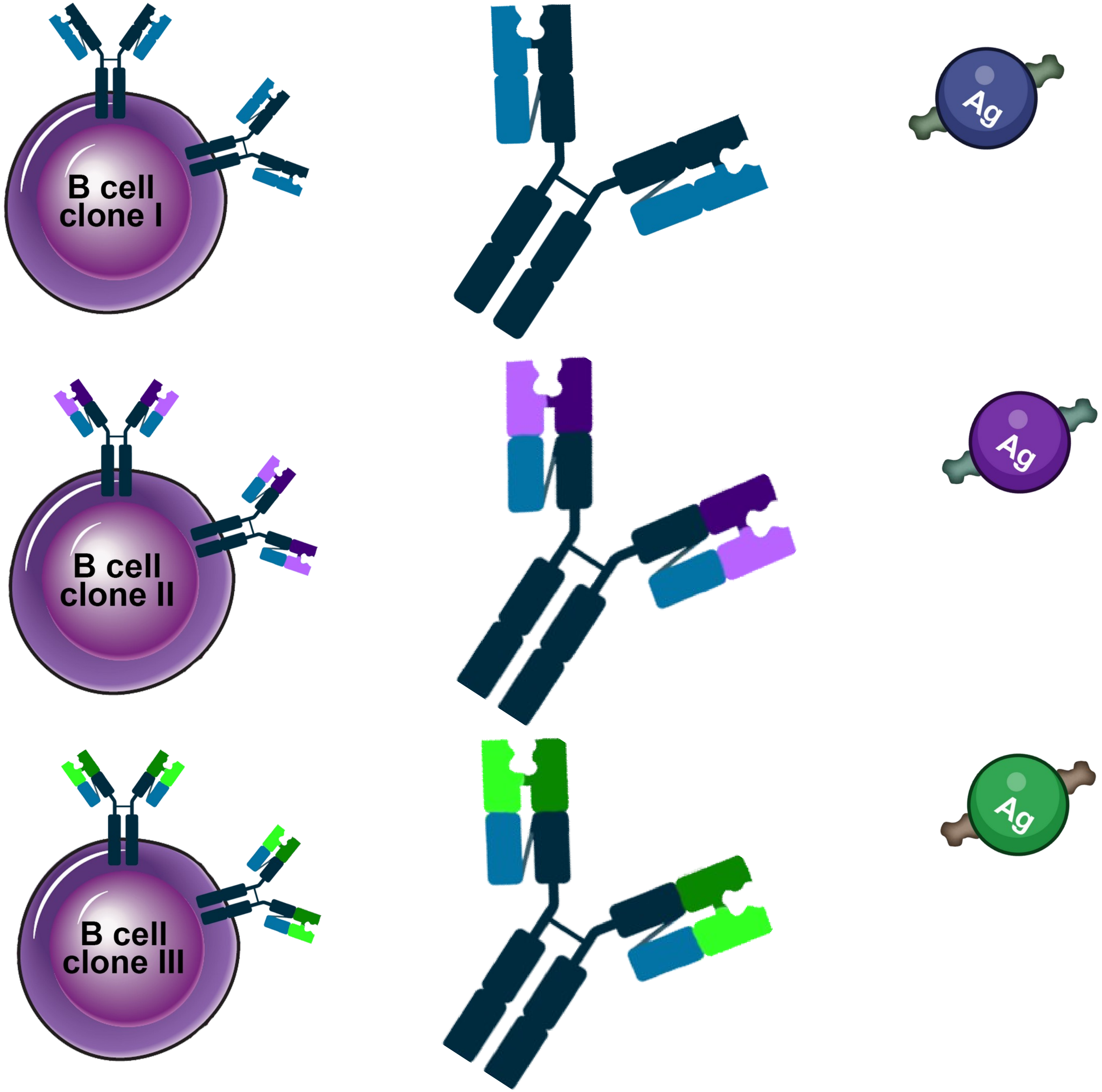
Main membrane bound Ig on mature B cell

**Secreted IgD**

بلا وظيفة







نحضر ضده

بطريقة صناعية نحضرها في المعمل

Monoclonal Abs

وحيدة النسيلة

# Monoclonal Abs(Mc Abs)

**Definition**

صناعيا

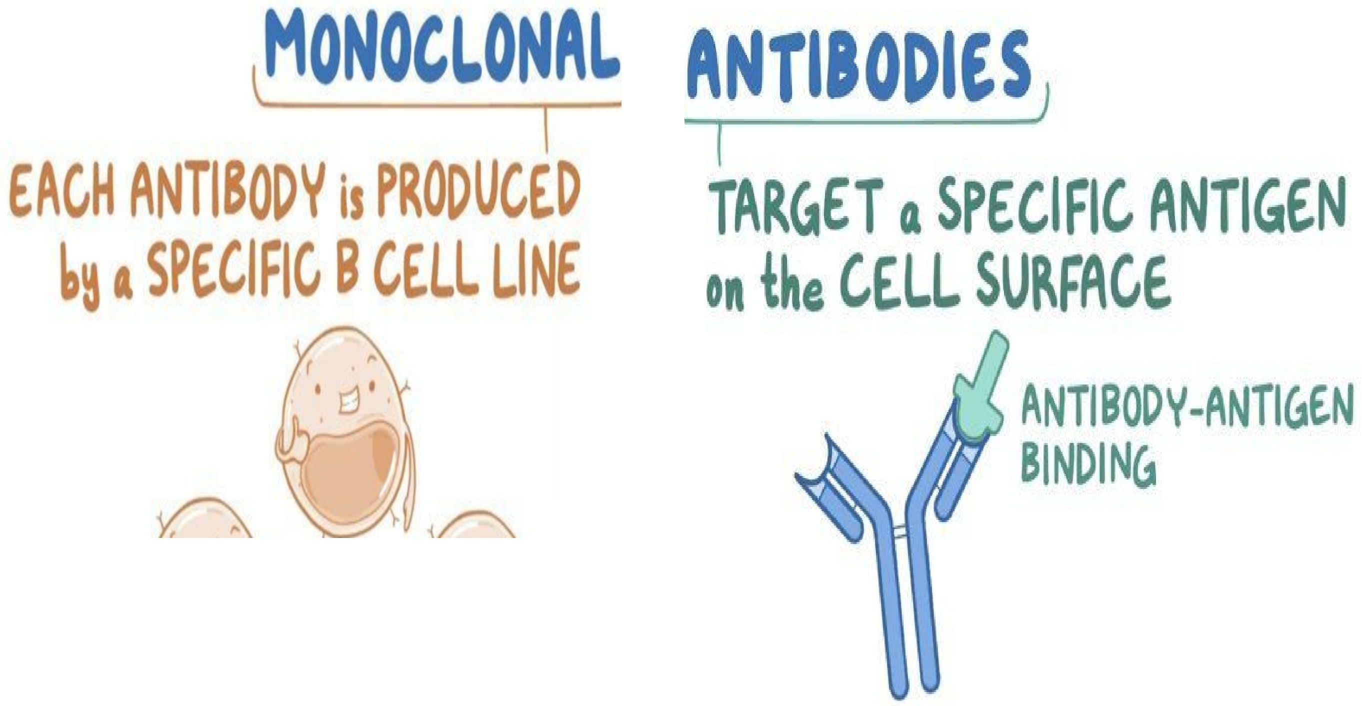
خارج الجسم

Ab produced artificially (in vitro)

by a single clone of B cell

↓

Specific for a single epitope


MONOCLONAL
ANTIBODIES
EACH ANTIBODY is PRODUCED by a SPECIFIC B CELL LINE
TARGET a SPECIFIC ANTIGEN on the CELL SURFACE
ANTIBODY-ANTIGEN BINDING

# Monoclonal Abs

## Method of production

طريقة الانتاج

المطلوب نوع واحد

B cells producing the desired single kind Ab

تندمج

are fused with tumor cells (myeloma cells)

سرطان في lymphocytes

↓

Production of hybridoma cells

خلايا مهجنة

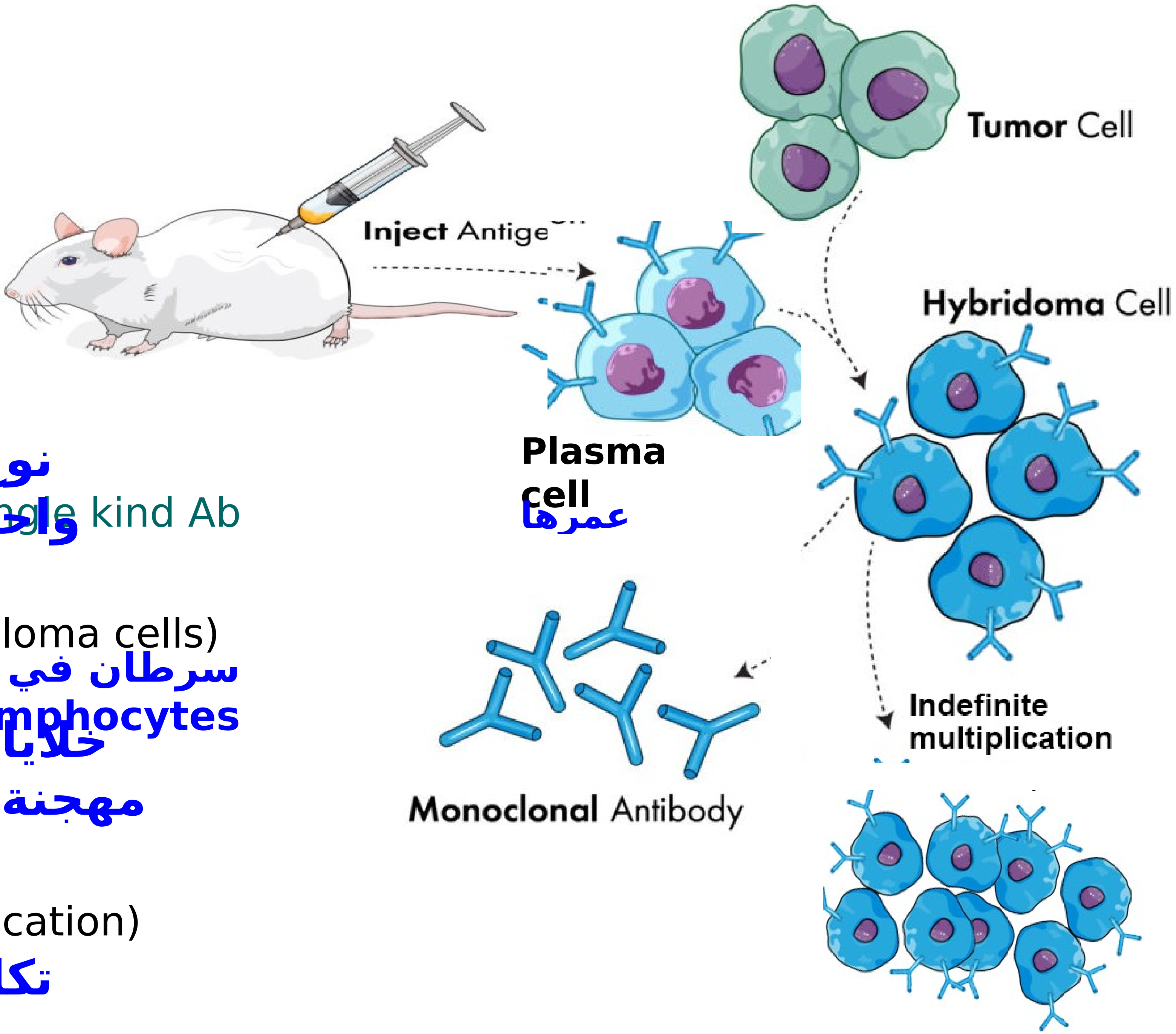
↓

المطلوب

1) Secrete the desired Mc Ab

2) Long lived (indefinite multiplication)

عمرها طويل لا نهائي تكاثر



# SUGGESTED TEXTBOOKS

**Basic Immunology**

**Functions & Disorders of the Immune System**

5th edition

Abul K.Abbas

*Chapter 8 : Effector mechanisms of Humoral immunity*